A Dissertation on

# A STUDY ON PARAMETERS OF HEPATORENAL DYSFUNCTION IN CASES OF DCLD AT A TERTIARY CARE CENTRE

Submitted to

**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY**

**CHENNAI – 600032**

*In partial fulfilment of the Regulationsfor the Award of the Degree of*

**M.D. BRANCH - I**

**GENERAL MEDICINE**


**DEPARTMENT OF GENERAL MEDICINE**

**STANLEY MEDICAL COLLEGE**

**CHENNAI – 600 001**

**MAY 2018**

# CERTIFICATE BY THE INSTITUTION

This is to certify that **Dr. K. VIJAYARAJAN,** Post – Graduate Student (May 2015 TO April 2018) in the Department of General Medicine STANLEY MEDICAL COLLEGE, Chennai- 600 001, has done this dissertation on "**A STUDY ON PARAMETERS OF HEPATORENAL DYSFUNCTION IN CASES OF DCLD AT A TERTIARY CARE CENTRE"** under my guidance and supervision in partial fulfillment of the regulations laid down by the Tamilnadu Dr. M. G. R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in May 2018.

**Prof. Dr. P.Vasanthi M.D**
**Professor and HOD**
**Department of General Medicine**
**Govt. Stanley Medical College**
**Chennai 01**

**Prof. Dr. S. Ponnambala Namasivayam**
**M.D, D.A, DNB**
**Dean**
**Govt. Stanley Medical College**
**Chennai 01**

## CERTIFICATE BY THE GUIDE

This is to certify that **Dr. K. VIJAYARAJAN,** Post - Graduate Student (MAY 2015 toMAY 2018) in the Department of General Medicine STANLEY MEDICAL COLLEGE, Chennai- 600001, has done this dissertation on "**A STUDY ON PARAMETERS OF HEPATORENAL DYSFUNCTION IN CASES OF DCLD AT A TERTIARY CARE CENTRE"** under my guidance and supervision in partial fulfilment of the regulations laid down by the Tamilnadu Dr.M.G.R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in May 2018.

**Prof.Dr.Hariharan**

Guide

Department of General Medicine,

Govt. Stanley Medical College & Hospital,

Chennai – 600001.

## DECLARATION

I, **Dr. K. VIJAYARAJAN,** declare that I carried out this work on **"A study on Parameters of Hepatorenal Dysfunction in cases of DCLD at a Tertiary Care Centre"** at the department of General Medicine and Medical Gastro Enterology of Government Stanley Hospital . I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, or diploma to any other university, board either in India or abroad.

This is submitted to The Tamilnadu DR. M. G. R. Medical University, Chennai in partial fulfilment of the rules and regulation for the M. D. Degree examination in General Medicine.

**Dr.K. VIJAYARAJAN**

## ACKNOWLEDGEMENT

At the outset I thank our dean **DR. S. PONNAMBALA NAMASIVAYAM, MD,DA,DNB.** for permitting me to carry out this study in our hospital.

I express my profound thanks to my esteemed Professor and Teacher **Dr. P.VASANTHI, M.D.,** Professor and HOD of Medicine, Stanley Medical College Hospital, for encouraging and extending valuable guidance to perform and complete this dissertation.

I express my sincere gratitude to my Guide **Prof. Dr. HARIHARAN**,a teacher par excellence, a constant source of inspiration for me,who also has helped at each and every step in the completion of this dissertation.

I immensely thank my unit Assistant Professor **Dr.SUGANYA, M.D.,** for her constant encouragement and guidance throughout the study.I would also like to extend my heartfelt thanks to **Dr. SATHYA, M.D.,** Assistant Professor for their guidances in completing this dissertation.

I sincerely thank the members ofInstitutional Ethical Committee, Stanley Medical College for approving my dissertation topic.

I thank all my colleagues, House Surgeons, and Staff nurses and other paramedical workers for their support.

At this juncture I would also want to extend my heartfelt gratitude to my parents **Mr. A. KRISHNAN and Mrs. ALAMELU** for the motivation and encouragement extended by them which gave fulfilment to the dissertation work.

I sincerely thank all those **patients** who participated in this study, for their co-operation.

Above all, I thank the **Almighty** for gracing me this opportunity, health, and knowledge throughout this study.

# A STUDY ON PARAMETERS OF HEPATORENAL DYSFUNCTION IN CASES OF DCLD AT A TERTIARY CARE CENTRE

# CONTENTS

## INTRODUCTION

Decompensated liver disease is most common Medical problem in our Country. Commonest causes of development of cirrhosis are alcohol, Hepatitis Virus (B&C) and other metabolic causes. Cirrhotic patient will develop various complications if not on proper treatment like UGI bleed due to esophageal varix, Hypatic encephalopathy, spontaneous bacterial peritonitis, Hepato renal syndrome. Coagulopathy and Hepato pulmonary syndrome, Hepatocellular caricinoma.

Study concentrated on parameters of hepto renal dysfunction. Cystation C is a early marker of development of hepatorenal syndrome in DCLD patient. Cystatin C is nonglycosylated low molecular wt. protein of the cystatin super family of cysteine protease inhibitors. Normal range (0.5-1.5mg./ dl) Cystatin C levels raised before rise of other renal parameters like creatinine, urea. Serum creatinine levels have limitations in cirrhotic patient usually low levels in DCLD pt due to ↓ synthesis & ↓ production due to muscle mass ↓, Drugs, presence of high bilirubin.

Cystatic C independent of muscle mass, age, gender not influenced by serum bilirubin & malignancy, cystatin C levels measurement more advantages

and early marker for development of renal dysfunction in DCLD patient and prevent the development of end stage renal disease.

## AIMS OF THE STUDY

1.**A study on parameters of Hepatorenal Dysfunction in cases of DCLD at a Tertiary Care Centre**

**2.To study the complication of DCLD**

**PRIMARY OBJECTIVE**- Role of cystatin C in Hepatorenal Dysfunction case of Cirrhosis.

**SECONDARY OBJECTIVES**-

1.To study the prevalence of causes of DCLD

2.To study the frequency of complication of DCLD

3.To study the advantages of Cystatic over Serum creatinine by using eGFR

**JUSTIFICATION OF STUDY**-

DCLD is major health problem among males in India most commonest cause of death in DCLD is HRS. It is very important to study early marker of AKI in DCLD patient. Serum creatinine levels have limitations in cirrhotic

patient usually low levels in DCLD pt due to ↓ synthesis & ↓ production due to muscle mass ↓, Drugs, presence of high bilirubin.

## REVIEW LITERATURE

### DECOMPENSATED LIVER DISEASE

Patient with chronic liver disease can present with acute decompensation due to various causes.

The decompensation may take the form of any of the following complications:

- Esophageal variceal bleeding
- Ascites
- Spontaneous bacterial peritonitis
- Hepatic encephalopathy
- Hepatorenal syndrome
- Coagulopathy
- Hepatocellular carcinoma
- Hepatopulmonary syndrome

CIRRHOSIS

Cirrhosis defined as irreversible chronic injury of the hepatic parenchyma and include extensive fibrosis in association with formation of regenerative nodules. Cirrhosis classified as

- Micronodular cirrhosis (<3mm)
- Macronodular cirrhosis (>3mm)

Causes of cirrhosis:

Alcoholism (60-70%)

Chonic viral hepatitis (10%)

- Hepatitis B
- Hepatitis C

Autoimmune hepatitis

Non alcoholic hepatitis

Biliary cirrhosis(5-10%)

- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Autoimmune cholangiopathy

Cardiac cirrhosis

Inherited metabolic live disease

- Hemochromatosis
- Wilson’s disease
- Alpha 1 antitrypsin deficiency
- Cystic fibrosis

Cryptogenic cirrhosis

COMPLICATIONS OF CIRRHOSIS

**1) HEPATO RENAL SYNDROME**

**History :**

Freriechs and Flint (1861-63) reported an association between advanced liver disease and a type of renal impairment that is characterized by oliguria, the absence of proteinuria, and normal renal histology.

In 1932, Helvig and Schultz introduced the term ‘a liver and kidney syndrome’.

Epstein et al demonstrated the importance of splanchnic and systemic vasodilation together with renal vasoconstriction as a foundational concept in the pathopathology of HRS.

## DEFINITION

HRS is a distinct form of functional acute/subacute renal failure characterised by severe renal vasoconstriction which develops in decompensated cirrhosis or acute liver failure in the absence of an underlying renal pathology.

Causes of renal failure in cirrhosis:

- Large volume paracentesis
- Shock
- Sepsis
- Nephrotoxic drugs
- Intrinsic renal disease
- Volume depletion secondary to diuretics

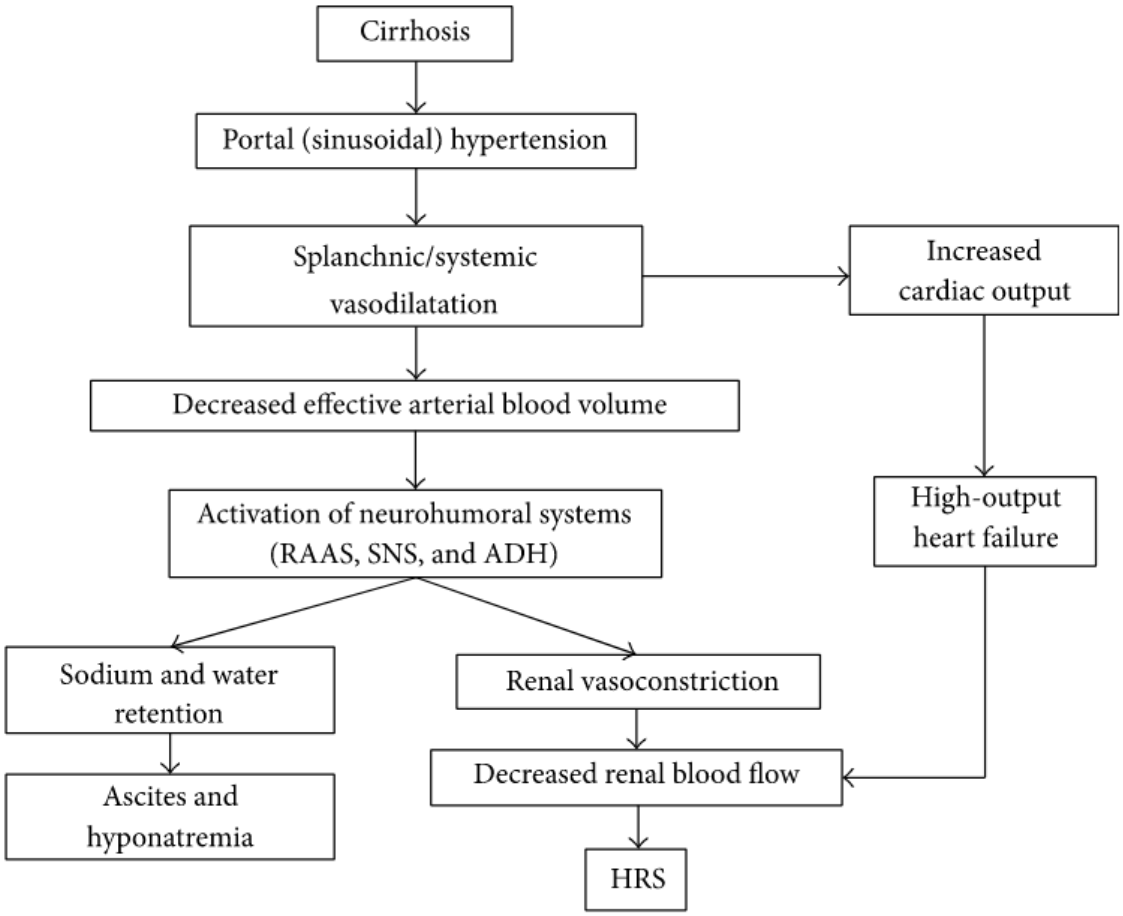
## EPIDEMIOLOGY

In patients admitted with DCLD ,

- 18% develops HRS by one year and
- 39 % by five years.

## PATHOPHYSIOLOGY OF HRS:

The peripheral arterial vasodilation theory is the most widely accepted explanation for the pathophysiology of HRS, which proposes that splanchnic vasodilation that occurs as a consequence of portal hypertension with cirrhosis is the inciting factor for the development of HRS. Splanchnic vasodilation is mediated principally by nitric oxide but also to a lesser extent by other vasodilator substances such as carbon monoxide, glucagon, vasodilator peptides, and others.



## PRECIPITATING FACTORS FOR HRS:

- Gastro intestinal bleed
- Large volume paracentesis, without albumin
- Bacterial infection
- Spontaneous bacterial peritonitis
- Acute alcoholic hepatitis

Types of HRS:

Type 1 : Cirrhosis with rapidly progressive acute renal failure , cr > 2.5

Type 2 :Cirrhosis with subacute Renal failure, cr > 1.5

Type 3: Cirrhosis with type 1 or 2 HRS superimposed on chronic kidney disease / acute renal injury

Type 4: Fulminant hepatic failure with HRS

## DIAGNOSTIC CITERIA:

HRS is a diagnosis by exclusion.

### Major Criteria

(i)Chronic or acute liver disease with advanced hepatic failure and portal hypertension.

(ii)Low GFR as indicated by serum creatinine > 1.5 mg/dL or 24 hr creatinine clearance < 40 mL/min.

(iii)Absence of shock, on-going bacterial infection, and current or recent treatment with nephrotoxic drugs and absence of gastrointestinal fluid losses (repeated vomiting or intense diarrhoea) or renal fluid losses (weight loss > 500 g/day for several days in patients with ascites without peripheral edema or 1000 g/day in patients with peripheral edema.

(iv)No sustained improvement in renal function (decrease in serum creatinine ≤ 1.5 mg/dL or increase in creatinine clearance to ≥ 40 mL/min) following diuretic withdrawal and expansion of plasma volume with 1.5 L of isotonic saline.

(v)Proteinuria < 500 mg/dL and no sonographic evidence of obstructive uropathy or parenchymal renal disease.

**Minor Criteria**

(i)Urine volume < 500 mL/day.

(ii)Urinary sodium < 10 mEq/L.

(iii)Urinary osmolality greater than plasma osmolality.

(iv)Urine red blood cells < 50 per high power field.

(v)Serum sodium < 130 mEq/L.

**TREATMENT:**

General management:

- Type 1 HRS – Hospitalisation
- Type 2 HRS – Outpatient

CVP for assessing fluid status

Stoppage of diuretics.

Tense ascites – paracentesis

- If >5 L fluid removed, then albumin is a good volume expander

Low salt diet,

Free water restriction (for hyponatremic cases)

HRS type 1 and 4 need intensive care

**THERAPEUTIC OPTIONS**

- Pharmological treatment
- Surgical
- TIPS

- Artificial liver support
- Liver transplantation
- LKT

## MEDICAL TREATMENT

### Treatment of hepatorenal syndrome.

| Drug | Dose |
|---|---|
| Terlipressin | • Bolus: 0.5–2.0 mg intravenously every 4–6 hours, with stepwise dose increments if there is no improvement of serum creatinine, to a maximum of 12 mg/day or the occurrence of complications, in combination with albumin.<br>• Continuous infusion: 4 mg/day with stepwise dose increments if there is no increase in mean arterial blood pressure >10 mmHg or improvement in serum creatinine level, up to a maximum of 12 mg/day or the occurrence of complications, in combination with albumin. |
| Noradrenaline | • Continuous infusion with a starting dose of 0.5 mg/h, with stepwise increments if there is no increase in mean arterial blood pressure >10 mmHg or improvement of serum creatinine level, up to a maximum of 3 mg/h or the occurrence of complications, in combination with albumin. |
| Midodrine plus octreotide | • Oral midodrine 7.5–12.5 mg three times daily to increase mean arterial blood pressure >10 mmHg. |

| Drug | Dose |
| --- | --- |
| | • Octreotide 200 μg subcutaneously three times daily. |
| Albumin | • 1 g albumin/kg body weight on the first day, followed by 200–400 g daily. |

**Prophylaxis against hepatorenal system.**

- Prompt and adequate treatment of hypovolemic situations
- Albumin substitution in spontaneous bacterial peritonitis (SBP)
- Albumin substitution with large-volume paracentesis
- Antibiotic prophylaxis in patients at increased risk of SBP
- Withdrawal of β-blockers in patients with cirrhosis with recurrent and refractory ascites
- Withdrawal of nonsteroidal drugs in portal decompensation
- Nephroprophylaxis in patients with cirrhosis when radiologic studies using contrast medium are performed

**Liver transplantation:**

- Treatment of choice for type 1 and 2 HRS.
- HRS disappears in the first month of transplantation

- Cyclosporine avoided in first few days after transplantation
- 3 year survival
    - 60% in patients with HRS
    - 70-80% in patients without HRS

## Scoring systems used in cirrhosis:

## 1.Child-Pugh score:

**CHILD-PUGH CLASSIFICATION OF CIRRHOSIS**

| | | Points Toward Total Score | | |
|---|---|---|---|---|
| **Factor** | **Units** | **1** | **2** | **3** |
| Serum bilirubin | μmol/L | <34 | 34–51 | >51 |
| | mg/dL | <2.0 | 2.0–3.0 | >3.0 |
| Serum albumin | g/L | >35 | 30–35 | <30 |
| | g/dL | >3.5 | 3.0–3.5 | <3.0 |
| Prothrombin time | seconds prolonged | <4 | 4–6 | >6 |
| | INR[a] | <1.7 | 1.7–2.3 | >2.3 |
| Ascites | | None | Easily controlled | Poorly controlled |
| Hepatic encephalopathy | | None | Minimal | Advanced |

[a]International normalized ratio.

***Note:*** The Child-Pugh score is calculated by adding the scores for the five factors and can range from 5 to 15. The resulting Child-Pugh class can be A (a score of 5–6), B (7–9), or C (≥10). Decompensation indicates cirrhosis, with a Child-Pugh score of ≥7 (class B). This level has been the accepted criterion for listing a patient for liver transplantation.

**2)Model for End-Stage Liver Disease (MELD) system:**

The MELD score is a prospectively derived system designed to predict the prognosis of patients with liver disease and portal hypertension. This score is calculated from three noninvasive variables:

- the prothrombin time expressed as the international normalized ratio (INR),
- the serum bilirubin level, and
- the serum creatinine concentration.

MELD = 3.8 [serum bilirubin (mg/dl)] + 11.2[INR] + 9.6 [serum creatinine (mg/dL)] + 6.4

**CYSTATIN C (or) CYSTATIN 3:**

- Cystatin C is a non-glycosylated basic protein encoded by the CST3 gene on the short arm of chromosome 20.
- It was first described as ‘gamma-trace’ in 1961 as a trace protein in CSF and urine of patients with renal failure
- Grubb and Lofberg first reported its aminoacid sequence. It was first proposed as a measure of GFR by Grubb and coworkers in 1985
- It is mainly used as a biomarker of kdney function.

- Normal levels in blood are 0.5 to 1.5 mg/dL. Levels vary with increasing age. It is found in all tissues and body fluids
- It is a potent inhibitor of liposomal proteinases and one of the most important extracellular inhibitor of cysteine proteases
- Recently it has been studies for its role in predicting new onset cardiovascular disease
- It also involves roles in brain disorders like amyloid, Alzheimer's disease
- GFR is a marker of kidney function, it is most accurately measured by injecting compounds such as inulin, radioisotopes, such as Uronium EDTA, $I^{125}$, $Tc^{99}$ DTPA
- These techniques are complicated, costly, time consuming and have side effects
- Creatinine is most widely used as a biomarker of kidney function. It is inaccurate in mild renal impairment
- Levels can vary with muscle mass, but not with protein intake
- Urea levels may change with protein intake
- Formulas such as Cockroft-Gault formula and MDRD formula try to adjust for these variables
- Cystatin C low molecular weight (13.3 kilo Daltons) and it is removed from the blood stream by glomerular filtration in kidney
- If kidney function and GFR reduces, the blood levels of Cystatin C rises

- Cystatin C levels are less dependant on age, sex, race and muscle mass compared to creatinine
- Cystatin C levels have been reported to be altered in patients with cancer, thyroid dysfunction and corticosteroid therapy
- Levels seem to be increased in HIV infection, which may sometimes be mistaken as renal failure
- Cigarette smoking and levels of C-reactive protein influence Cystatin-C

**Other roles:**

- Mutation in the cystatin 3 gene are responsible for a type of cerebral amyloid angiopathy a condition predisposing to stroke, ICH, dementia
- Cystatin C also binds amyloid Beta and reduces its aggregation and deposition if it is a potent target in Alzheimer's. Cystatin C is higher in Alzheimer's disease
- Role of cystatin C in multiple sclerosis remains controversial
- Cystatin C levels are decreased in atherosclerotic and aneurismal lesion of the aorta
- Cystatin C has investigated for prognostic marker of several forms of cancer

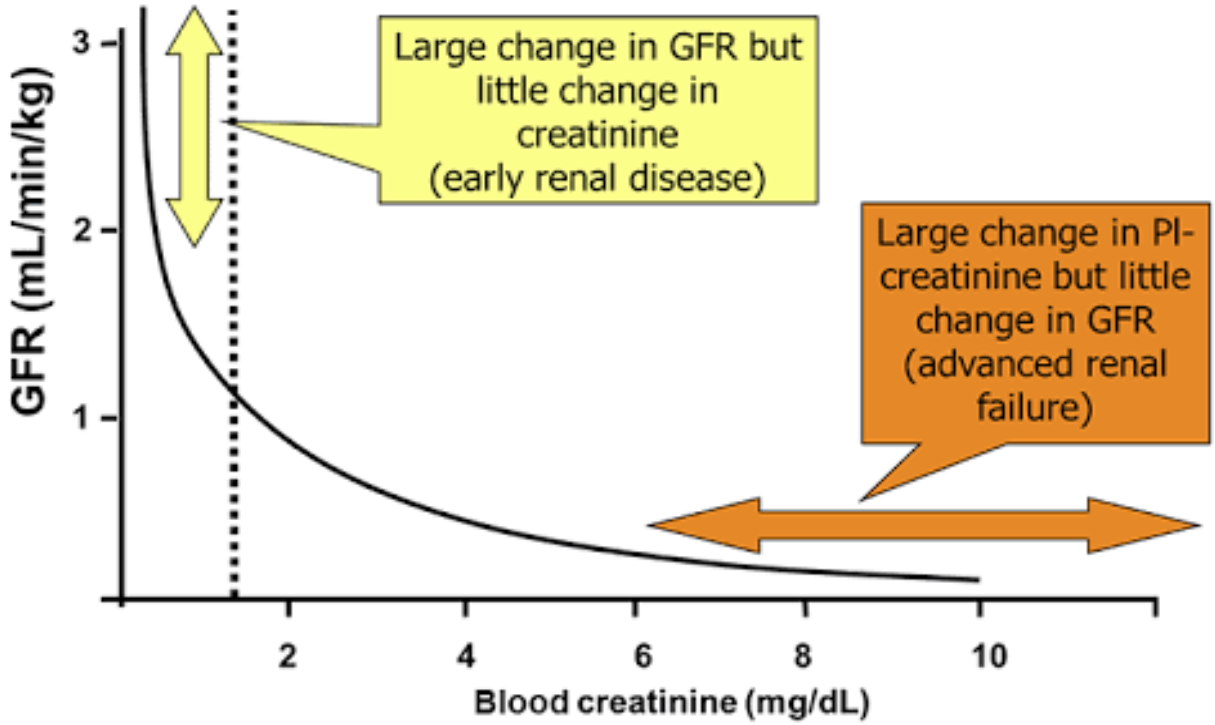
## CREATININE

Creatinine is a metabolic product of creatine derived mainly from myocytes and dietary meat. The typical daily production rates are 20 to 25 mg/kg/day in men and 15 to 20 mg/kg/day in women. Persons with high muscle mass will be having high creatinine production, compared to those with low muscle mass. The normal range for creatinine is reported between 0.4 and 1.5mg/dL. Kidney eliminates creatinine mainly by glomerular filtration and, to a lesser extent, by proximal tubular secretion .Glomerular filtration rate accounts for more than 90% of creatinine elimination. Creatinine is not absorbed or metabolized to any significant amount in kidney.

Creatinine is clinically more used to track kidney function, as it accumulates when renal elimination is compromised. An increase in creatinine suggests a reduction in GFR. Likewise, a decrease in creatinine suggests an improvement in GFR. It is important to understand that a change in plasma creatinine does not always correlate with decline in renal function in a linear fashion (diagram 1) ie A small increase in creatinine at a lower creatinine level may signals greater decline in renal function, compared to same increase in creatinine when the baseline creatinine levels are high.

Creatinine is not a perfect marker due to the variable contribution of tubular secretion of creatinine. When the renal function declines, tubular secretion of creatinine increases. Because of this, creatinine based estimation of GFR can overestimate renal function because of the increasing proportion of creatinine eliminated by tubular

secretion in renal failure.  In addition to that, intra-laboratory variation are also present for measurement of creatinine.




**UREA**

Urea elimination by kidney is more complex than that of  creatinine. This is what renders blood urea nitrogen as not a useful marker of kidney function .Elevation in blood urea nitrogen may be due to many reasons like gastrointestinal bleeding, steroid use and parenteral nutrition . Reduction in blood urea nitrogen can be seen in malnutrition and liver disease. Blood urea nitrogen will become more informative when the ratio of BUN: creatinine exceeds 20:1.It will give clue regarding pre renal AKI.

## CLEARANCE

Clearance means “quantity of fluid which completely cleared of a marker over a definite period of time.” It is commonly expressed in mL per minute. Marker for clearance should be biologically inert, freely and completely filtered by the glomerulus. It should be neither secreted nor absorbed by tubules. It should not be degraded by the kidney. GFR can be calculated from the measurements of the markers’ clearance with the help of an ideal marker.

ie GFR=($U_{marker}$ × volume of urine/$P_{marker}$)1440

$U_{marker}$ concentration of the marker in the urine.

Volume of urine is the volume produced over 24 hours(in mL)

$P_{marker}$ concentration of the marker in the plasma.

Value of 1440 has been used to convert the units to mL per minute.(1440 minutes in 24 hours).

The classic gold standard marker for the measurement of creatinine clearance is inulin. But, many substances has been superceded inulin such as iothalamate, diethylenetriamine, pentaacetic acid, iohexal ethylene diamine tetra acetic acid. These substances are very useful in the accurate measurement of GFR. They used to use in special circumstances which require more precision than estimates from creatinine clearance.

## CREATININE CLEARANCE

Creatinine clearance is not an ideal marker due to the contribution from tubular secretion. But it can be measured easily and can be used clinically to estimate GFR. Creatinine clearance can be done through equation based estimations or by 24 hour urine collection. Following equations are the most commonly used equations based on creatinine to find out the kidney functions in adults

1. Cockcroft-gault equation
2. MDRD formula

**COCKCROFT – GAULT EQUATION**

Estimated creatinine clearance =(140-age)×weight in kg×0.85(if female)/72×plasma creatinine.

This formula originally developed to use in male inpatients .But, later found to be useful in other populations too.

The main drawbacks of this equation

1. difficult to measure the actual lean body weight of the patient

2. overestimation of true GFR with creatinine clearance with lower levels of kidney function.

**MDRD EQUATION**

*Estimated GFR=186×(Scr)$^{-1.154}$×(age)$^{-0.203}$*0.742(if female)*1.21(if African American)*

The MDRD formula originally found out in established outpatient CKD patients using iothalamate renal clearance as reference. MDRD formula correlates good in CKD patients with GFR<60mL/min/1.73m$^{2.}$.But there are certain situations where 24 hour urine collection is better than MDRD formula.

1. GFR>60 ml/min/1.73 m$^2$.
2. Age < 18 and > 70
3. Extremely body size
4. Severe malnutrition
5. Pregnancy
6. Skeletal muscle disease
7. Paraplegia or quadriplegia
8. Vegetarian
9. Rapid change in renal function
10. advanced kidney disease

MDRD formula has been adjusted for African American population but not for Hispanics or Asian popoulations. MDRD formula primarily developed in white population not having diabetic kidney disease.

Both these equations might be less accurate in populations with different ethnicities outside the united states.

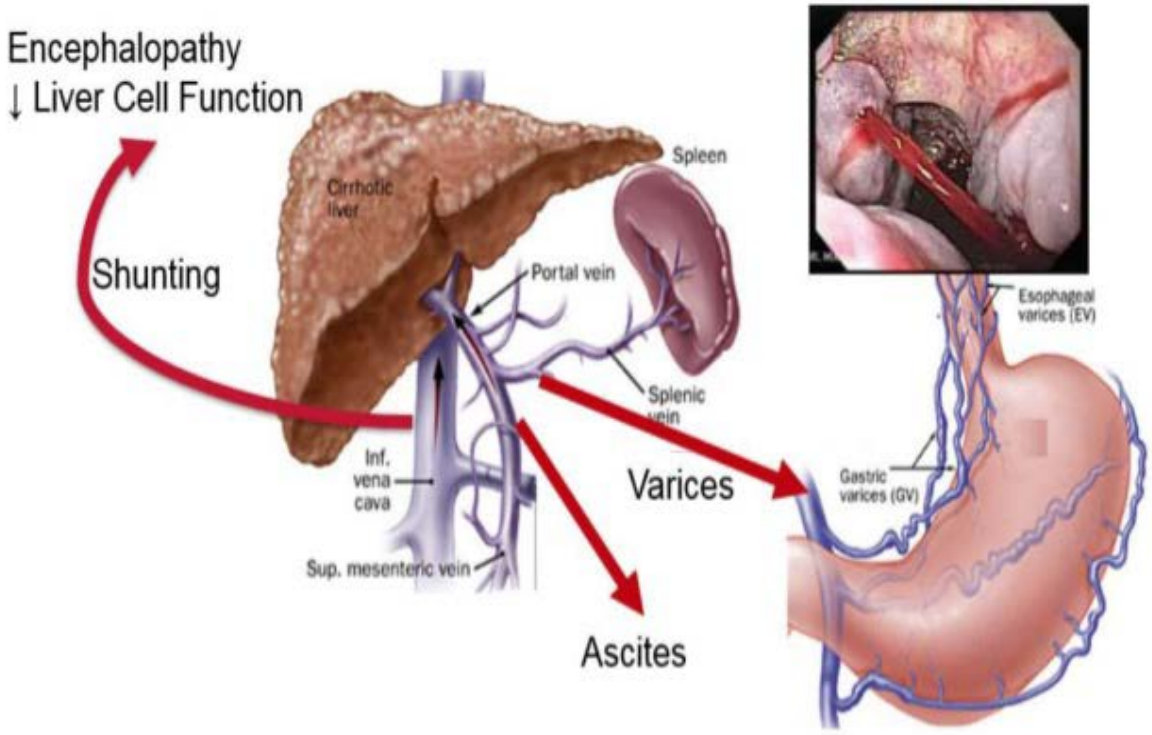
## OESOPHAGEAL VARICEAL BLEED

### Definition of a variceal bleed

- Oesophageal varices are dilated oesophageal veins secondary to portal hypertension.

### Causes of variceal bleeds

- Pre-hepatic
  - o Portal vein thrombosis / obstruction
  - o Increased portal blood flow: fistula
- Hepatic
  - o Cirrhosis
    - ☐ 90% of cirrhotic patients get varices, 30% bleed
  - o Acute hepatitis (esp. alcoholic)
  - o Schistosomiasis
  - o Congenital hepatic fibrosis
- Post-hepatic
  - o Compression (e.g. from tumour)
  - o Budd-Chiari syndrome
  - o Constrictive pericarditis (and rarely right-sided heart failure)




**Management of variceal bleeds**

- Resuscitation

  o ABC

  - ☐ Oxygen, blood tests (VBG, FBC, U+Es, LFTs, clotting, X-match)
  - ☐ Erect CXR
  - ☐ Fluid resuscitation
  - ☐ HDU/ITU
  - ☐ Monitoring

- CVP line and catheter
- Correct anaemia and coagulopathy

  o Transfusion trigger should be 7 (aim 7-9)

☐ Using a trigger of 9 significantly increases mortality at 45 days (NEJM 2013).

- •Terlipressin (glypressin) 2g IV

o Vasopressin analogue. Reduces portal pressure. Contraindicated in shock and peripheral vascular disease

- Octreotide (a somatostatin analogue)
- Antibiotics

o Broad spectrum. IV Tazocin 4.5g. Blood is an excellent culture medium so these patients often end up septic without antibiotics. It may also be a subacute bacterial infection that has brought the patient into hospital initially.

- Endoscopy (once stable and not bleeding)
- Band ligation

☐ This is the first choice of treatment

**Sclerotherapy**

☐ In this therapy the varices are sclerosed

☐ Various sclerosants can be used

☐ Complications include transient fever, dysphagia, chest pain, ulceration and stricture.

**Variceal obturation with glue**

☐ This involves embolisation of varices with a glue-like substance (N-butyl-2-cyanoacrylate)

☐ Particularly good for gastric or gastro-oesophageal variceal bleeding

☐ However, there is a risk of embolisation to the lung, spleen or brain

**Transjugular intrahepatic portosystemic shunt (TIPSS)**

o Where bleeding is not controlled by endoscopy

o Patient needs to be transferred to a specialist liver unit

o Hepatic vein is cannulated percutaneously via the internal jugular vein using a needle under ultrasound guidance and a tract is created through the liver from the hepatic to the portal vein reducing portal pressure.

o High success rate but encephalopathy found in 25% cases (as portal blood diverted from the liver) and shunt occludes within 1 year in up to 50% cases

- Prevention of variceal bleeding

1. Beta blockers

☐ These lower portal blood pressure and risk of further bleeding by reducing portal blood flow.

2. Nitrates

☐ Just for secondary prophylaxis.

☐ Nitrates can also be used in the acute variceal haemorrhage with vasopressin and terlipressin.

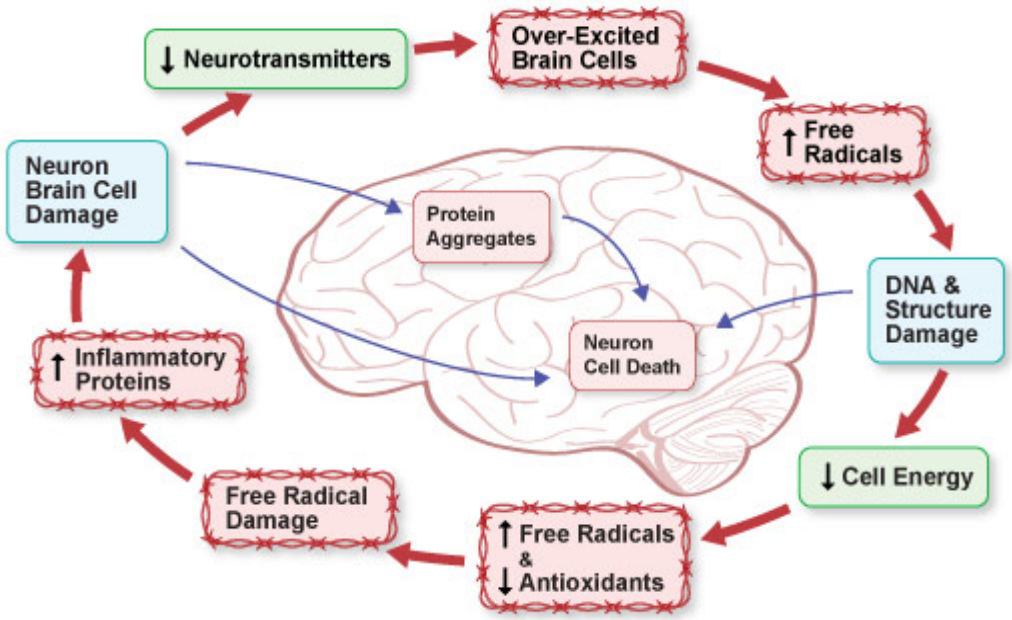
3. Endoscopic screening

☐ All patients with newly-diagnosed cirrhosis should have screening endoscopy, looking for oesophageal varices. In the long-term, repeated endoscopic screening is usually required, e.g. 2 to 3-yearly in cases of small varices.

## HEPATIC ENCEPHALOPATHY

Common precipitants of hepatic encepalopathy

- Renal failure
- Gastrointestinal bleeding
- Infection
- Constipation
- Sedative drugs e.g. opiates, benzodiazepines, antidepressants and antipsychotic drugs
- Diuretics
- High protein intake



**Presentation of hepatic encepalopathy**

- Mild

  o Impairment of attention and decision-making, and may have impaired fitness to drive. These patients usually have normal function on standard mental state testing but abnormal psychometric testing.

- Moderate

1. Confusion
2. Asterixis
3. Fetor hepaticus
4. Hypothermia
5. Hyperventilation

- Severe

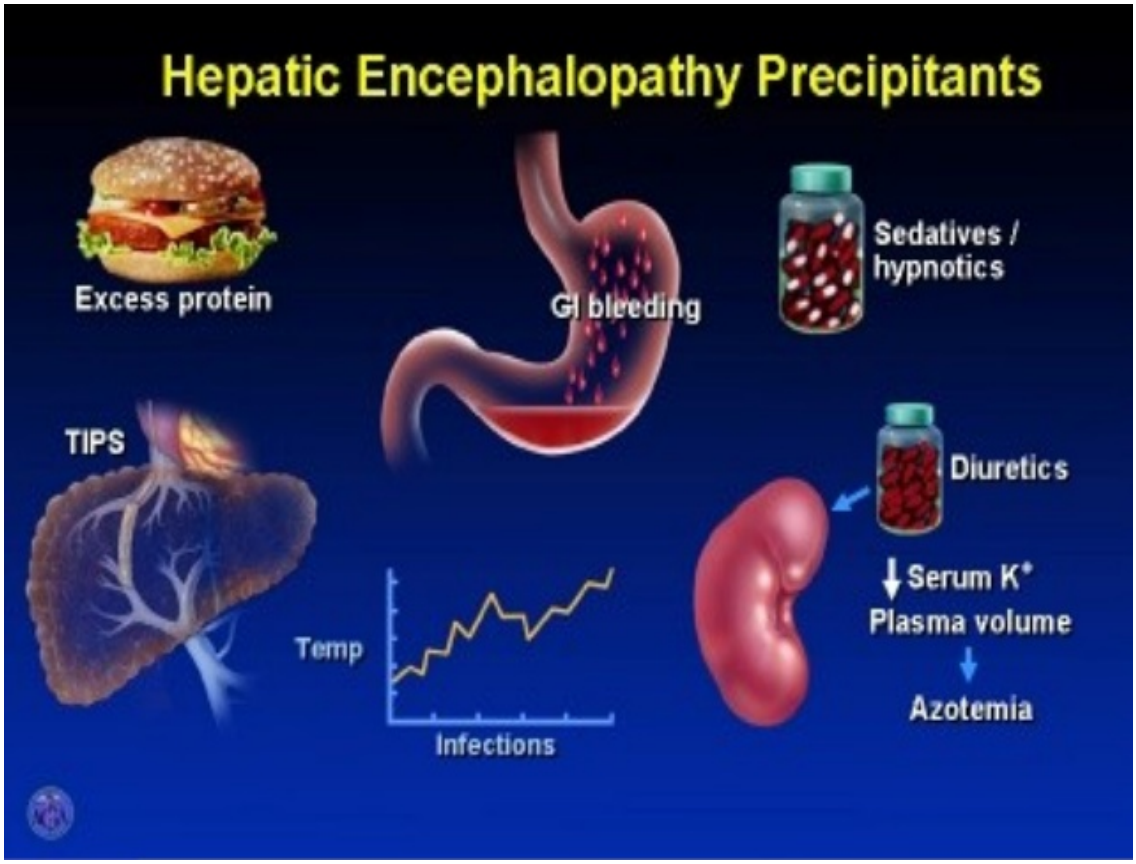
  Coma with or without response to painful stimuli

| |
|---|
| • Grade 0: subclinical; normal mental status, but minimal changes in memory, concentration, intellectual function, coordination. |
| • Grade 1: mild confusion, euphoria or depression, decreased attention, slowing of ability to perform mental tasks, irritability, disorder of sleep pattern such as inverted sleep cycle. |
| • Grade 2: drowsiness, lethargy, gross deficits in ability to perform mental tasks, obvious personality changes, inappropriate behaviour, intermittent disorientation. |
| • Grade 3: somnolent but rousable, unable to perform mental tasks, disorientation to time and place, marked confusion, amnesia, occasional fits of rage, speech is present but incomprehensible. |
| • Grade 4: coma, with or without response to painful stimuli. |

**Investigations in hepatic encepalopathy**

- Full septic screen
- Ascitic tap to check for SBP
- DRE to check for faecal impaction
- Ammonia levels are raised and can help with diagnosis. The sample needs to be collected and then stored on ice and sent directly to the laboratory.
- EEG

  o High-amplitude low-frequency waves and triphasic waves - not specific for hepatic encephalopathy.
- MRI/CT can help to exclude other causes of altered mental function such as intracranial lesions
- Visual evoked responses show classic patterns associated with hepatic encephalopathy.




**Management of hepatic encepalopathy**

- Lactulose or enemas

  - To clear the nitrogen load

- Antibiotics

  - To stop nitrogen breakdown

    ☐ Metronidazole

  - Prophylactic antibiotics

    ☐ Rifaximin 550mg twice daily is licensed for prevention of hepatic encephalopathy

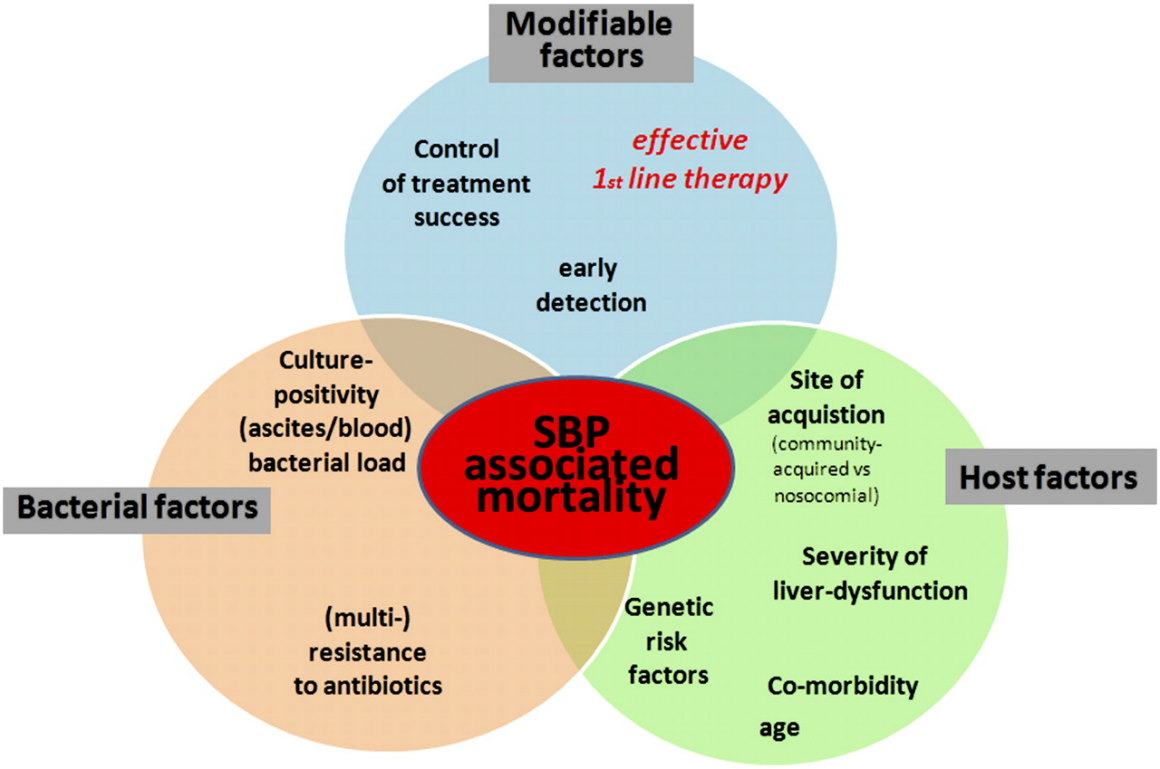
**Spontaneous bacterial peritonitis (SBP)**

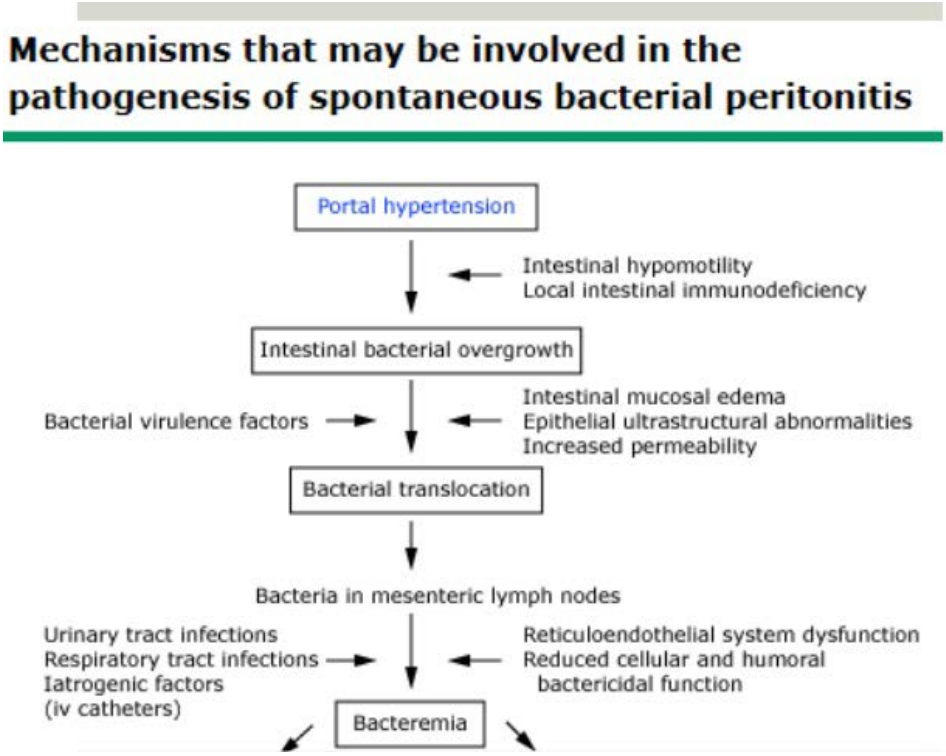
**Epidemiology of SBP:**

- 10-30% of patients with ascites and has mortality rate of 20%.
- Organisms are usually E. coli, streptococci and enterococci.

Symptoms of spontaneous bacterial peritonitis (SBP)

- Generalised abdominal pain
- Hepatic encephalopathy, renal impairment or peripheral leucocytosis without any obvious precipitating factor.






Investigations in suspected SBP

- Diagnostic paracentesis

  - Mandatory in all patients with cirrhosis requiring hospital admission

  - Ascitic fluid contains >250 cells/mm.

Treatment spontaneous bacterial peritonitis (SBP)

- Prompt broad spectrum iv antibiotics

  - e.g. Tazocin 4.5g three times daily

  - Treat as soon as ascitic tap has been sent if high index for suspicion

- If fluid resuscitation needed for septic shock then try to avoid colloid/crystalloid and use plasma expander such as human albumin solution instead.

- Good evidence for prophylactic antibiotics after one episode of SBP

  - E.g. Ciprofloxacin 250mg twice daily

## SUPPORTING LITERATURES

Several studies have been published regarding advantage of Cystatin C over Serum creatinine.

1. Study was conducted in Department of Medicine and Nephrology, INHS Asvini, Colaba, Mumbai, Maharastra, India during from September 2008 to September 2010 at a tertiary care hospital. The study group consisted of 200 healthy subjects and 130 patients of AKI. After obtaining an informed consent, a screening questionnaire was filled to collect information such as age, gender, height, weight, comorbidities, personal history, drug history, presenting complaints, and laboratory investigations. A detailed physical examination was carried out.

The serum cystatin C and serum creatinine values were measured simultaneously and analyzed. In the AKI study group, they were taken within 24 hours of onset of injury. The “RIFLE” criteria were used for defining the AKI, and the stages “risk” and “injury” constituted the “early AKI.”

GFR was estimated using the Cockcroft-Gault formula for creatinine clearance and Larsson formula for cystatin C-based GFR.

Larsson formula: $eGFR = 77.24 \times \text{cystatin } C^{-1.2623}$

The gold standard for measuring GFR viz. inulin clearance, urinary clearance of exogenous radioactive markers ($^{125}$I-iothalamate and $^{99m}$Tc-DTPA (diethylene-triamine -pentaacetate)), was not used in this study due to practical limitations.

Statistical analysis was performed using appropriate statistical tests and *P* value less than 0.05 was considered significant.

Demographic and biochemical characteristics of study population

Serum cystatin C had lower standard deviation (1.1) and serum creatinine had higher standard deviation (1.8) in AKI indicating lesser variability of serum cystatin C.

The variation of serum creatinine was significantly greater than that of serum cystatin C in both groups. The standard deviation of serum creatinine (0.23) is double that of serum cystatin C (0.12) in the healthy group, which indicates a wide fluctuation in serum creatinine compared to serum cystatin C in healthy population too.

Although the correlation between serum creatinine and serum cystatin C was significant in both groups, a high strength of correlation was observed in the AKI group. This implies that small changes in serum creatinine are best reflected by a proportionate rise in serum cystatin C in AKI, especially at lower values.

Correlation between serum creatinine and serum cystatin C

In our study, it was found that in the AKI group majority (56.2%) had normal creatinine values (0.9–1.4 mg/dl). This subset was in “creatinine blind” range where serum creatinine values are normal with elevated cystatin C levels. All 130 patients with AKI had deranged cystatin C levels. This confirms the finding that serum cystatin C is elevated much before serum creatinine levels start rising and does not suffer from the disadvantage of creatinine blind area. In this way it helps for early detection of kidney injury.

2. A total of 192 patients were enrolled in our cohort with cirrhosis and AKI. Of these, 106 had at least 2 blood samples collected and were included in this study. Samples were not collected in the remaining 86 patients either due to failure to consent to blood collection or initiation of dialysis prior to obtaining consent. Baseline demographic, clinical, and laboratory characteristics for the entirety of study participants and the four groups designated by trends in creatinine and cystatin C are shown in . There were no significant differences in any demographic variables or in those relating to the patients' liver disease between those patients who did and did not have serum samples collected. The mean patient age was 56.3 and 66% were male. Thirty-seven (35%) patients met the primary composite endpoint during their hospitalization. Of these, 28 patients died and 22 required dialysis, with 13 of these experiencing both

dialysis and death. On sensitivity analysis, there was no difference in death, 28/106 (26%) versus 22/86 (26%), or the composite of death or dialysis, 37/106 (35%) versus 30/86 (35%), between those patients with and without blood samples obtained. The majority of patients had advanced cirrhosis evidenced by previously suffered complications including ascites, 76%, hepatic encephalopathy, 63%, variceal bleeding, 23%, and SBP, 12%. Reasons for admission were similar between the four groups. The median Child-Pugh score was 10 and MELD 26.4 at the time of enrollment. There was no difference in Child-Pugh and MELD scores across groups nor were serum sodium levels or the presence of hyponatremia at enrollment significantly different.

The Serum Cr and CysC levels were $1.04 \pm 0.1$ and $1.8 \pm 0.8$ mg/L, respectively. HRS developed in 18 patients during the follow-up period (6 months). Type 1 HRS was found in 5 patients and type 2 HRS was found in 13 patients with no significant difference between both types regarding baseline characteristics. Age ($p < 0.001$), albumin ($p < 0.001$), sodium ($p < 0.005$), cystatin C ($p < 0.001$), and e-$GFR_{MDRD}$ (estimated glomerular filtration rate—modification of the diet in renal disease) ($p < 0.007$) were significant dependent predictive factors for the development of HRS. The CysC level was the most independent predictive factor for HRS (OR, 2.1; 95% CI, 0.75–0.97; $p < 0.002$). Eighteen patients died during the follow-up period. Age ($p < 0.001$), INR ($p < 0.001$), e-$GFR_{MDRD}$ ($p < 0.03$), sodium ($p < 0.01$),

MELD score ($p < 0.05$), albumin ($p < 0.001$), and CysC ($p < 0.001$) levels were significant dependent factors for predicting mortality. CysC (OR, 5.3; $p < 0.006$) level and INR (OR, 1.01; $p < 0.006$) were the most independent factors for predicting mortality.

Serum cystatin C had lower standard deviation (1.1) and serum creatinine had higher standard deviation (1.8) in AKI indicating lesser variability of serum cystatin C.

The variation of serum creatinine was significantly greater than that of serum cystatin C in both groups. The standard deviation of serum creatinine (0.23) is double that of serum cystatin C (0.12) in the healthy group, which indicates a wide fluctuation in serum creatinine compared to serum cystatin C in healthy population too.

Although the correlation between serum creatinine and serum cystatin C was significant in both groups, a high strength of correlation was observed in the AKI group. This implies that small changes in serum creatinine are best reflected by a proportionate rise in serum cystatin C in AKI, especially at lower values.

In our study, it was found that in the AKI group majority (56.2%) had normal creatinine values (0.9–1.4 mg/dl). This subset was in “creatinine blind” range where serum creatinine values are normal with elevated cystatin C levels. All

130 patients with AKI had deranged cystatin C levels. This confirms the finding that serum cystatin C is elevated much before serum creatinine levels start rising and does not suffer from the disadvantage of creatinine blind area. In this way it helps for early detection of kidney injury.

Multiple logistic regression applied to GFR calculated by Cockroft-Gault using serum creatinine and GFR-calculated serum cystatin C in AKI group gave a correlation coefficient (*R*) of 0.822. This showed a good positive correlation between creatinine-based GFR and cystatin C-based GFR. Correlation coefficient of creatinine-based GFR is -0.00213 and that of cystatin C-based GFR is -0.00673. Cystatin C-based GFR resulted in more negative correlation compared to creatinine-based GFR in the AKI group. It means cystatin C-based GFR reflects a decline in GFR with worsening AKI in a much better way compared to creatinine-based GFR. The *P* value was significant ($P < 0.01$) for both cystatin C- and creatinine-based GFR.

Thus in the AKI group, cystatin C-based GFR was better compared to creatinine-based GFR in early detection of worsening clinical status. This suggests the utility of serum cystatin C over serum creatinine in predicting early decline in GFR and thereby helping in early therapeutic intervention.

3. Study was conducted in the Department of internal medicine, Eulji University School of Medicine Seol, Korea, study done by Miyeon Chung, Dae Won Jun, and Su Ah Sung et al…

The mean age of 53 cirrhotic patients was 59 years, with 38 males and 15 female patients. Hepatitis B virus-related hepatitis was the most common cause of liver cirrhosis among the patients (39.6%), followed by alcoholic hepatitis (30.2%), hepatitis C virus-related hepatitis (5.7%), non-alcoholic steatohepatitis (5.7%), and unknown causes (18.9%). Ascites was found in 35 patients (66%). The average Child-Pugh score was 9.37±2.78, with Child-Pugh A consisting of 8 patients (15.1%), Child-Pugh B of 19 patients (35.8%), and Child-Pugh C of 26 patients (49.1%). The MELD score was 14.11±6.22, and the MELD-Na score was 16.41±7.48. The mean duration of follow-up was 13±8.9 months (average±standard deviation).

Creatinine clearance and the e-$GFR_{MDRD}$ showed a negative correlation with serum cystatin C [$r$=-0.532 ($p$<0.001) and $r$=-0.691 ($p$<0.001), respectively], but had no correlation with urine cystatin C and urine cystatin C/urine creatinine ratio [$r$=-0.129 ($p$=0.2) and $r$=-0.124 ($p$=0.3), respectively]. Serum cystatin C showed a positive correlation with the MELD and MELD-Na scores [$r$=0.346 ($p$=0.011) and $r$=0.427 ($p$=0.001), respectively] but had no correlation with the Child-Pugh score ($r$=0.234; $p$=0.09). Urine cystatin C was not correlated with

MELD score ($p$=0.108), MELD-Na score ($p$=0.123), or Child-Pugh score ($p$=0.5).

Nine out of the 53 patients with liver cirrhosis developed acute kidney injury during the first three months of follow-up. The e-$GFR_{MDRD}$ did not yield noticeable differences between the groups with and without acute kidney injury ($p$=0.18), but the formulae utilizing serum cystatin C, i.e., e-$GFR_{Hoek}$ and $GFR_{Larsson}$, differed significantly between two groups ($p$=0.03 and $p$=0.03, respectively).

To investigate the efficacy of serum creatinine and serum cystatin C in predicting acute kidney injury, the area under ROC curve was calculated. The results were 0.735 (95% CI, 0.525-0.945, $p$=0.028) for serum cystatin C and 0.698 (95% CI, 0.495-0.901, $p$=0.063) in creatinine. Using the ROC curve, the appropriate cutoff values of serum cystatin C and creatinine for predicting acute kidney injury were 1.23 mg/L (sensitivity 0.667, 1-specificity 0.136) and 0.9 mg/dl (0.85 mg/dl: sensitivity 0.778, 1-specificity 0.455; 0.95 mg/dl: sensitivity 0.556, 1-specificity 0.273), respectively. The sensitivity, specificity, positive predictive value, and negative predictive value of the cystatin C reference value in regard to renal injury occurring within three months were found to be 66.7%, 86.4%, 50%, and 92.7%, respectively. During the whole observation period, 17 patients (32.1%) were developed acute kidney injury. The average initial serum creatinine and cystatin C levels were 1.00 mg/dl and 1.30 mg/L among patients

showing acute kidney injury. The area under the ROC curve was 0.809 (95% CI, 0.671-0.947, $p<0.001$) in serum cystatin C and 0.719 (95% CI, 0.568-0.870, $p=0.011$) in creatinine.

4. Karina sofa, Silvia Coelho et all… Study was conducted patients admitted to the non surgical ED of the Fernando Fonseca Hospital from March to November 2008, Lisban Portugal. In this prospective cohort study, serum and urinary cystatin C were serially measured in a heterogeneous group of patients ($n = 616$) presenting to a tertiary care emergency department. The primary outcome was AKI, classified according to RIFLE and AKIN criteria. The secondary outcome was an adjudication based on clinical criteria to AKI, prerenal azotemia, chronic kidney disease (CKD), and normal kidney function.**Results:** Patients were adjudicated to have AKI in 21.1%, prerenal azotemia in 25.8%, CKD in 2.4%, and normal kidney function in 50.7%. For the diagnosis of AKI, the discriminatory ability of urinary creatinine and cystatin C was marginal. Both serum cystatin C and serum creatinine (at presentation and 6 hours later) showed high discriminatory ability for the diagnosis of AKI. However, only serum cystatin C attained a significant early predictive power (Hosmer-Lemeshow $P$ value > 0.05). Serum cystatin C could differentiate between AKI and prerenal azotemia, but not between AKI and CKD.**Conclusions:** Serum cystatin C is an early, predictive biomarker of AKI, which outperforms serum creatinine in the heterogeneous emergency

department setting. However, neither biomarker discriminated between AKI and CKD. Additional biomarkers continue to be needed for improved specificity in the diagnosis of community-acquired AKI.

## MATERIALS AND METHODS

This study was carried out in the Department of General Medicine and Department of Medical Gastro Enterology at Government Stanley Medical College and Hospital,Chennai during the period between April 2017-September 2017.This study was ethically approved by the Ethical Commitee of Government Stanley Medical College,Chennai

This study is a cross sectional study enrolling 50patient of DCLD with HRS.The patients were selected from Department of General Medicine and Department of Medical Gastro enterology during the study period.

## INCLUSION CRITERIA

- Patient age 18- 65 years
- Decompensated liver diseases of all etiology.

## EXCLUSION CRITERIA

- Known Renal Disease.
- Known Renal Transplant.

- Immunocompromised state.
- Past History of HRS.
- Past History of Nephrotoxic Drugs.

Applying all these criteria,50patient of DCLD with HRSwere selected and included in the study after taking their informed consent.

**METHODOLOGY**

Clinical sample and data was collected from -

1.Patients admitted in the Dept.of General Medicine with DCLD & HRS, Govt. Stanley Hospital, Department of Medical Gastro Entrology.

After screening, patients who fulfil inclusion criteria and showing willingness to participate in trial has been selected and included in study. A detailed history taking and clinical examination was done in all patients.

- Investigations,
    1. CBC,
    2. RFT, RBS, electrolytes
    3. LFT, PT, INR
    4. **Cystatin C**
    5. Urine Analysis

6. Viral Markers (HBsAg, Anti HCV)
7. Sr. Uric acid
8. USG Abdomen
9. ECG, X-ray chest
10. OGD scopy

Patients who has been selected for the study measured Cystatin C and Serum Creatinine Level compared by using cockroft gault formula. Results analysed and eGFR calculated by cockroft gault formula.

1. **Socio-demographic data :**

   Age

   Sex

   Occupation / Income

   Family history

   Life Style

   Alcohol

   Smoking

2. **Clinical examination**

   General Examination

   Systemic Examination

Abdomen : Hepato Splenomegaly

Shifting dullness

CVS : S1S2

Rs : Pleural effusion

CNS : Flaps

Vital

PR : BP :

## STATISTICAL ANALYSIS

Collected data was prepared into masterchart in Microsoft Excel and analysed statistically in SPSS software version 11.5.Results were considered if p value was below 0.05.

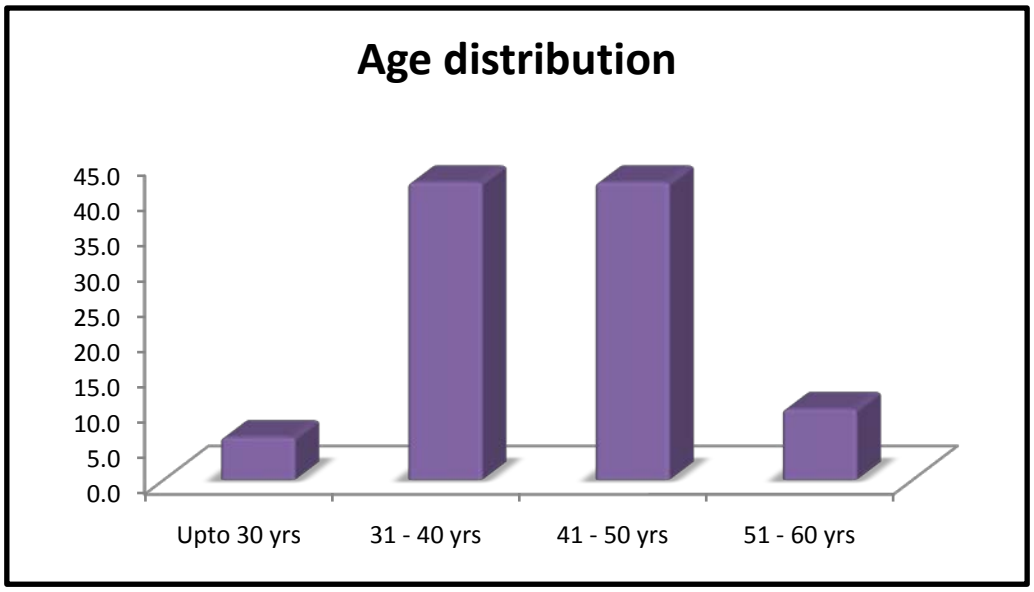
The collected data were analysed with IBM.SPSS statistics software 23.0 Version.To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables.To find the significance in categorical data Chi-Square test was used. In the above statistical tool the probability value .05 is considered as significant level**.**

## RESULTS

## 1. AGE DISTRIBUTION

| | | Frequency | Percent |
|---|---|---|---|
| Valid | Upto 30 yrs | 3 | 6.0 |
| | 31 - 40 yrs | 21 | 42.0 |
| | 41 - 50 yrs | 21 | 42.0 |
| | 51 - 60 yrs | 5 | 10.0 |
| | Total | 50 | 100.0 |

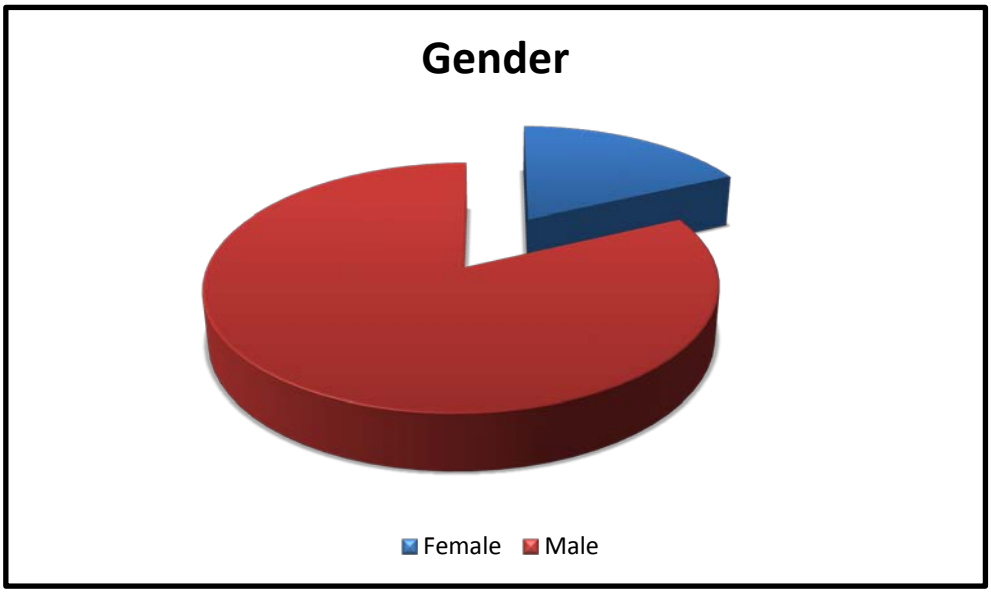
- The mean age of the sample was 41.40 and the age ranged between a 28-30 years with a standard deviation of 11.137



**2) SEX**

**Sex**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | Female | 9 | 18.0 |
| | Male | 41 | 82.0 |
| | Total | 50 | 100.0 |



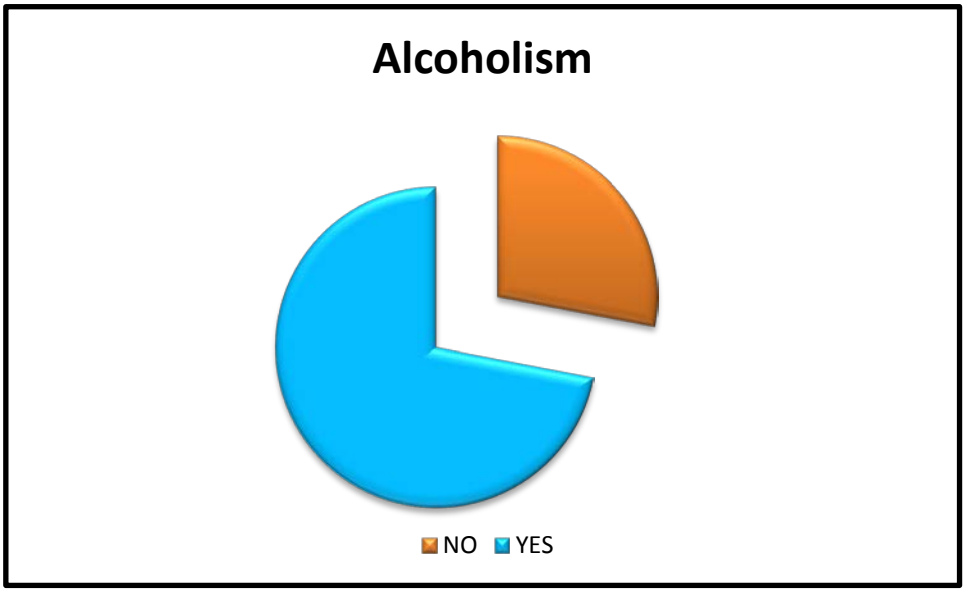

In this study 82% were male patients and 18% female

## 3. RISK FACTORS

## A) ALCOHOLISM

**Alcoholism**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 14 | 28.0 |
| | YES | 36 | 72.0 |
| | Total | 50 | 100.0 |




72% of the patients with DCLD were alcoholics

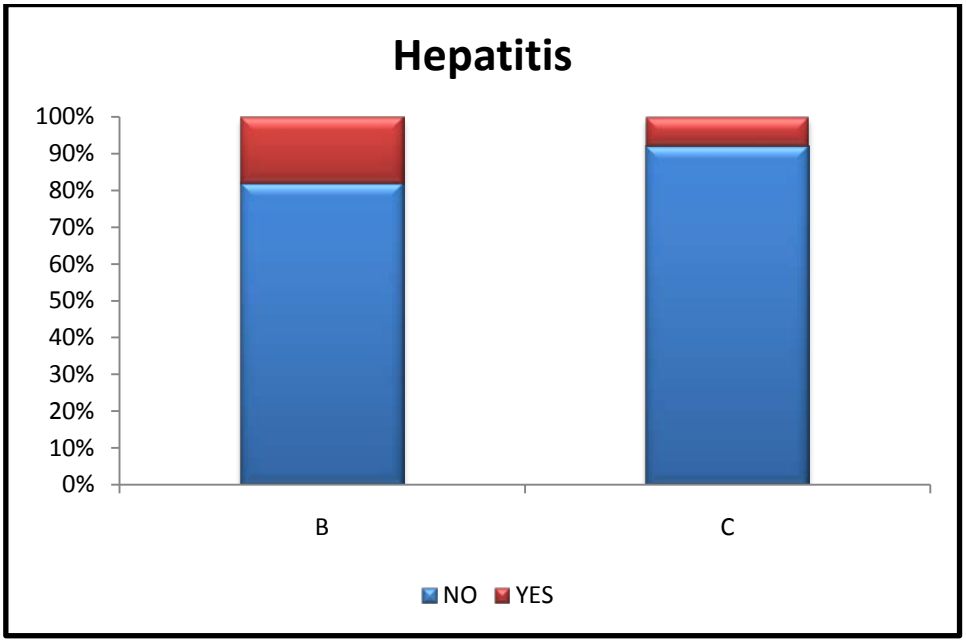
## B)VIRAL HEPATITIS

**Hepatitis B**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 41 | 82.0 |
| | YES | 9 | 18.0 |
| | Total | 50 | 100.0 |

**Hepatitis C**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 46 | 92.0 |
| | YES | 4 | 8.0 |
| | Total | 50 | 100.0 |



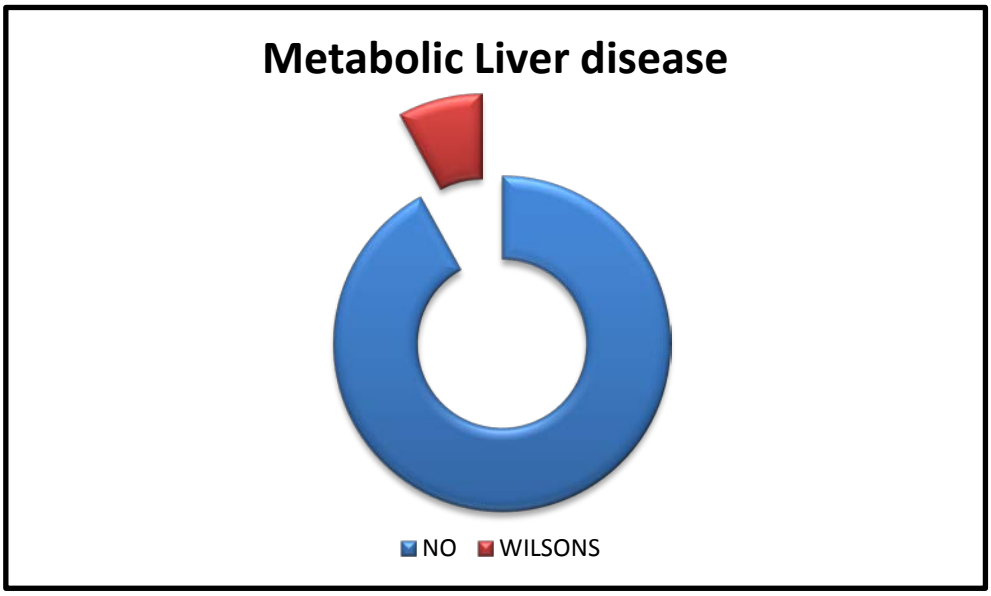

18% of the patient with DCLD were Hepatitis B positive

4% of the patient with DCLD were Hepatitis C Positive

## C)METABOLIC LIVER DISEASE

**Metabolic Liver disease**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 46 | 92.0 |
| | WILSONS | 4 | 8.0 |
| | Total | 50 | 100.0 |

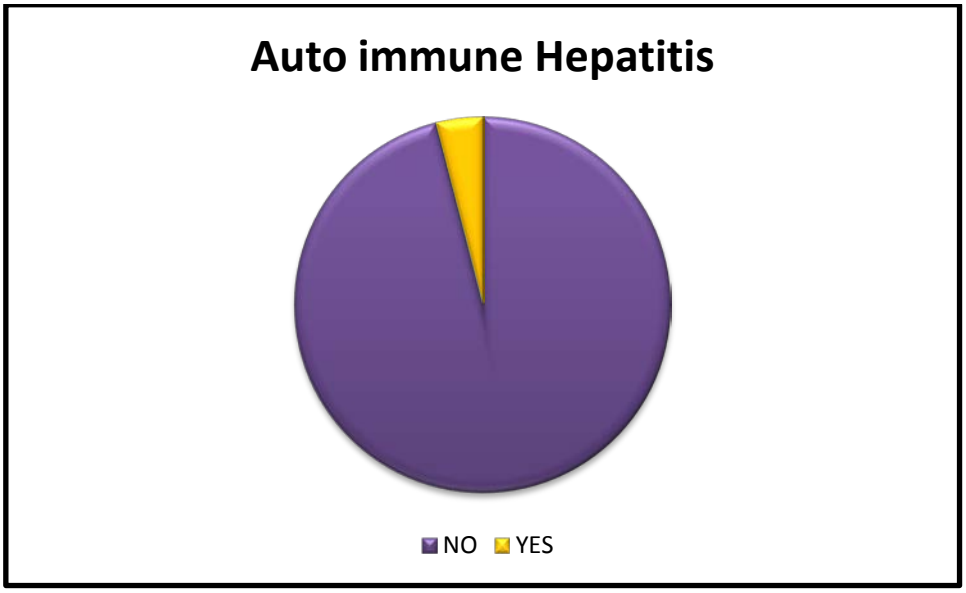



4% of patients with DCLD were Wilsons Disease

## D)AUTO IMMUNE HEPATITIS

**Auto immune Hepatitis**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 48 | 96.0 |
| | YES | 2 | 4.0 |
| | Total | 50 | 100.0 |




2% of patients with DCLD were Auto immune Hepatitis

## 4.COMPLICATIONS

### A) HRS

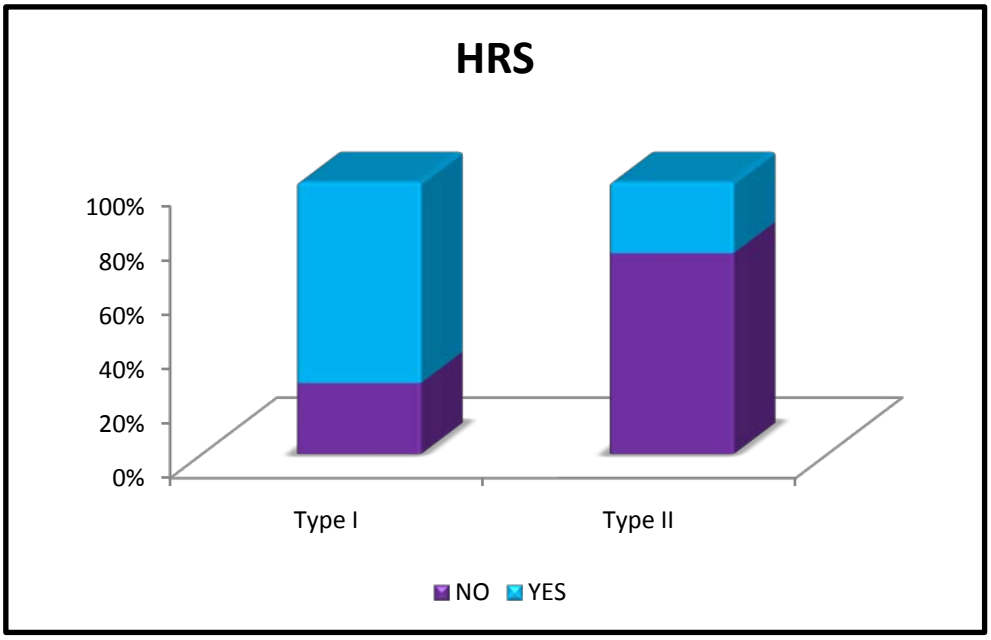
**HRS Type I**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 13 | 26.0 |
| | YES | 37 | 74.0 |
| | Total | 50 | 100.0 |

**HRS Type II**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 37 | 74.0 |
| | YES | 13 | 26.0 |
| | Total | 50 | 100.0 |

| | Type I | Type II |
|---|---|---|
| NO | 26.0 | 74.0 |
| YES | 74.0 | 26.0 |



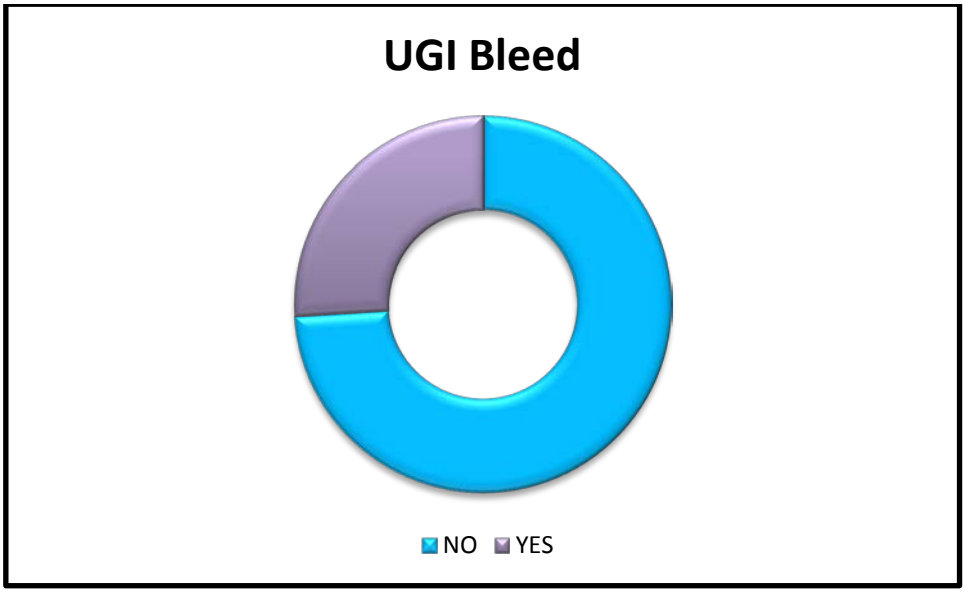

Among 50 DCLD patients 74% were type I HRS, 26% were type II HRS

Type I HRS more common than type II HRS

**B) UGI Bleed**

**UGI Bleed**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 37 | 74.0 |
| | YES | 13 | 26.0 |
| | Total | 50 | 100.0 |



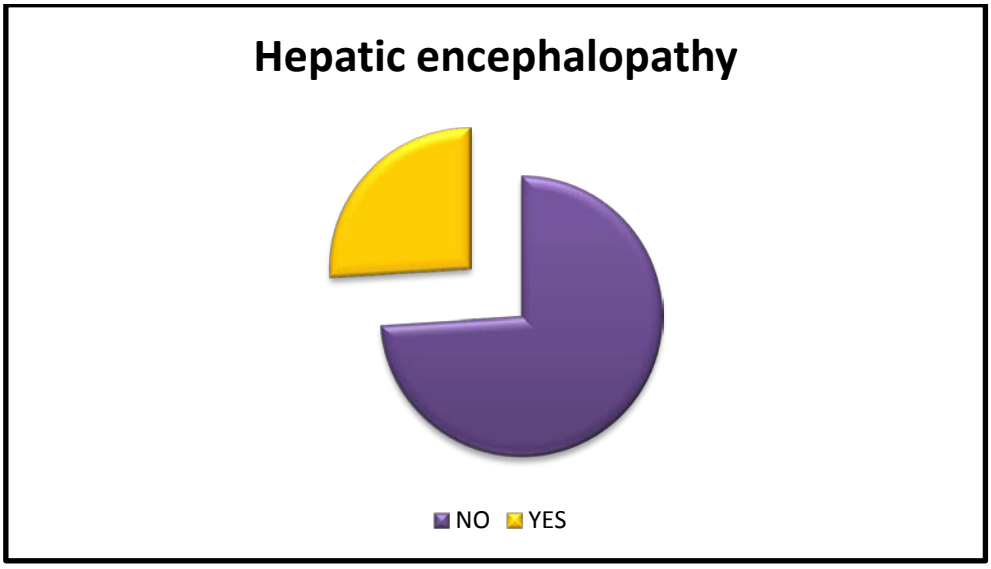

Among 50 DCLD with HRS patients 26% were developed UGI Bleed.

Type I HRS more common than type II HRS

## C) HEPATIC ENCEPHALOPATHY

**Hepatic encephalopathy**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 37 | 74.0 |
| | YES | 13 | 26.0 |
| | Total | 50 | 100.0 |

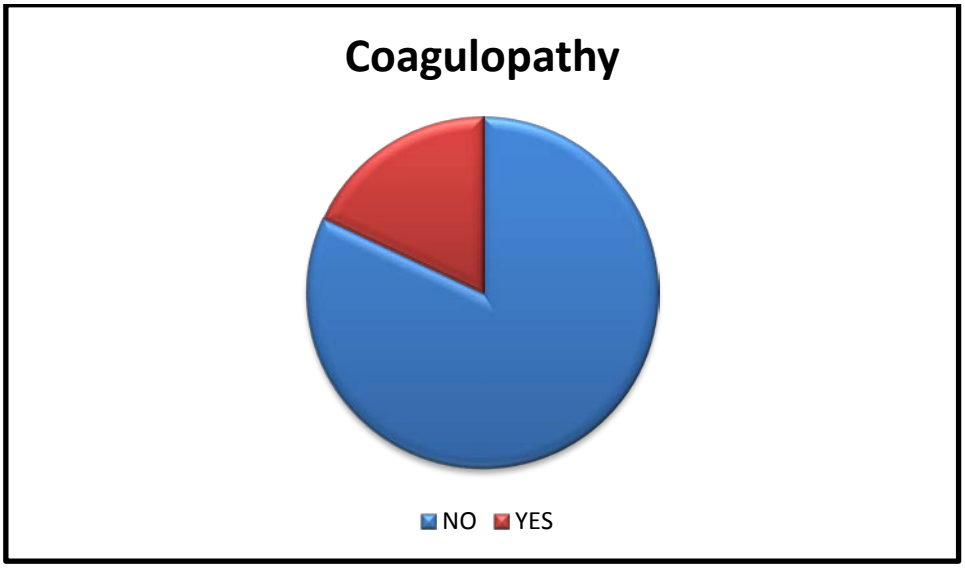



Among 50 DCLD patients 26% were developed Hepatic Encephalopathy

## D) COAGULOPATHY

**Coagulopathy**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 41 | 82.0 |
| | YES | 9 | 18.0 |
| | Total | 50 | 100.0 |

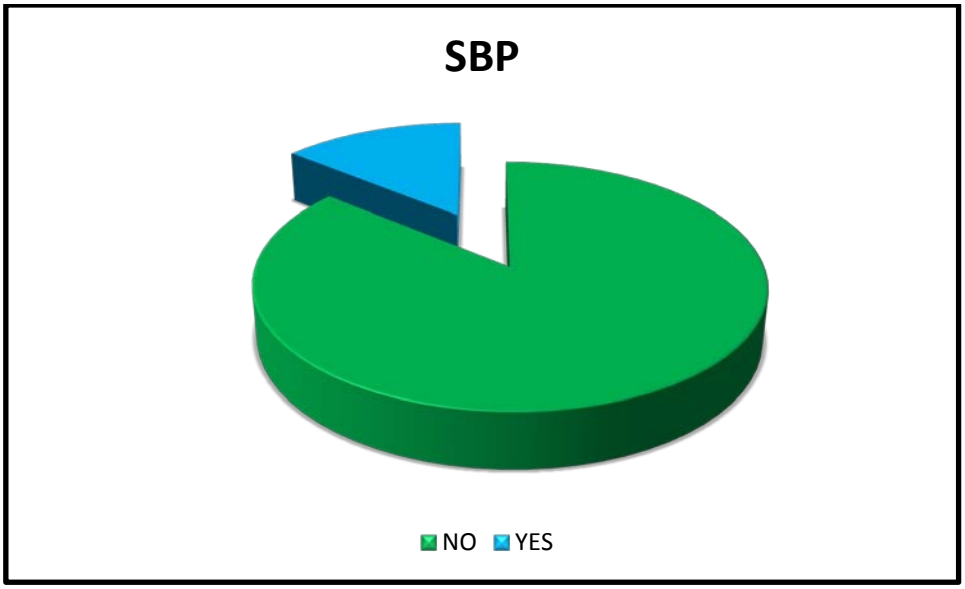



Among 50 DCLD patients 18% were developed Coagulopathy.

## E) SPONTANEOUS BACTERIAL PERITONITIS

**SBP**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 43 | 86.0 |
| | YES | 7 | 14.0 |
| | Total | 50 | 100.0 |

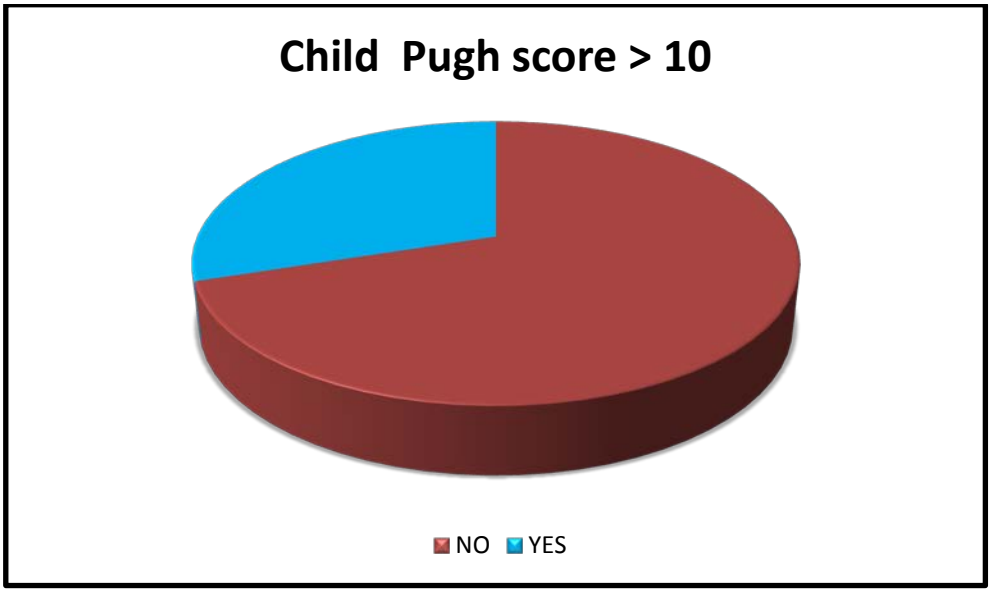



Among 50 DCLD patients 14% were developed Spontaneous Bacterial Peritonitis

## 5.CHILD PUGH SCORE

**Child Pugh score > 10**

| | | Frequency | Percent |
|---|---|---|---|
| Valid | NO | 35 | 70.0 |
| | YES | 15 | 30.0 |
| | Total | 50 | 100.0 |




In this study 30% of the patient having child pugh score >10

**Descriptive Statistics**

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Age | 50 | 28 | 60 | 41.40 | 7.253 |
| Cystatin C | 50 | .8 | 5.8 | 3.246 | 1.2209 |
| Serum Creatinine | 50 | 1.4 | 3.4 | 2.108 | .5082 |
| GRF | 50 | 51.1 | 86.1 | 70.862 | 9.6521 |
| Valid N (listwise) | 50 | | | | |

## Regression

| Variables Entered/Removed[a] | | | |
|---|---|---|---|
| Model | Variables Entered | Variables Removed | Method |
| 1 | Serum Creatinine, Cystatin C[b] | | Enter |

a. Dependent Variable: GRF

b. All requested variables entered.

| Model Summary | | | | |
|---|---|---|---|---|
| Model | R | R Square | Adjusted R Square | Std. Error of the Estimate |
| 1 | .785[a] | .616 | .600 | 6.1076 |

a. Predictors: (Constant), Serum Creatinine, Cystatin C

| ANOVA[a] | | | | | | |
|---|---|---|---|---|---|---|
| Model | | Sum of Squares | df | Mean Square | F | Sig. |
| 1 | Regression | 2811.812 | 2 | 1405.906 | 37.690 | .000[b] |
| | Residual | 1753.206 | 47 | 37.302 | | |
| | Total | 4565.018 | 49 | | | |

a. Dependent Variable: GRF
b. Predictors: (Constant), Serum Creatinine, Cystatin C

**Coefficients[a]**

| Model | | Unstandardized Coefficients | | Standardized Coefficients | t | Sig. | 95.0% Confidence Interval for B | |
|---|---|---|---|---|---|---|---|---|
| | | B | Std. Error | Beta | | | Lower Bound | Upper Bound |
| 1 | (Constant) | 97.835 | 3.721 | | 26.295 | .000 | 90.350 | 105.320 |
| | Cystatin C | -4.124 | .936 | -.522 | -4.407 | .000 | -6.007 | -2.242 |
| | Serum Creatinine | -6.444 | 2.248 | -.339 | -2.867 | .006 | -10.967 | -1.922 |

a. Dependent Variable: GRF

The derived regression equation is for the GRF is **GRF = - 4.12* Cystatin C - 6.44 * Serum Creatnine + 97.83** and both were found to be highly statistical significant influence with R square value 61.6 % with P = 0.01 < 0.05

## DISCUSSION

DCLD is one of the major cause of mortality across the world. In India DCLD affects males more common than females. In India DCLD is leading gastro intestinal cause of mortality in males. In this study mainly concentrated advantage of cystatin C compared to creatinine and complication of DCLD. HRS (hepatorenal syndrome) is one of the major complication that can leads to death of the patient. Because medical management does not helps to recover from HRS unless it is identified in a early stage.

HRS is basically a diagnosis of exclusion. There is no biochemical substance available to diagnose HRS.

Until now serum creatinine is the only renal parameter easily available & less cost parameter for diagnosing HRS. Serum creatinine is not a good markes for identify HRS at early stage.

Serum creatinine is not a ideal parameter to diagnose HRS. Because Serum creatinine dependent on various other factors like age, muscle mass, sex, drugs, high bilirubin.

It is essential to identify the HRS at early stage. Only parameter which is elevated before urea, creatinine is cystatin C.

Cystatin C raised in HRS at early stage before rising of renal parameters. Moreover Cystatin C not dependent on age, sex, muscle mass etc.,

In this study we found Cystatin C raised high levels eventhough serum creatine just above normal range. Study conducted at Government Stanley Medical College, Chennai over a period of 6 months to identify the advantage of Cystatin C over serum creatinine and commonest causes of DCLD, frequency of complications.

Among 50 patient 9 (18%) females and 41 (82% ) males. DCLD more common in males.

Risk factor (or) cause of DCLD, identified in this study were Alcohol (72%), Hepatitis B (18%), Hepatitis C (8%) metabolic liver disease (8%) Auto immune hepatitis (4%). Finally conclude Alcoholism is major cause for DCLD.

Among 50 HRS patient HRS type I (74%) is more common than type II HRS (26%)

We found HRS type II patient have developed other complications like Hepatic encephalopathy, UGI bleed, Coagulopathy, Spontaneous Bacterial peritonitis compared to HRS Type I.

USI bleed (26%), Hepatic encephalopathy (26%), Coagulopathy (18%), SBP (14%), Cystatin C highly elevated when GFR has minimally reduced, Serum Creatinine slowly rised when GFR reduced very low levels.

***Limitations of the study***

1. The sample size was small
2. The study duration was small
3. Our study did not have any data on mortality and recovery of the HRS patients.
4. Our study we did not have any data on commonest cause for DCLD among female patient because female patient included in this study was very small.

**CONCLUSIONS**

1. Our study showed that Cystatin C is better biochemical parameter than serum creatinine for calculating eGFR.
2. HRS type I more common than HRS type II
3. HRS type II associated with other complications of DCLD like UGI bleed, Hepatic encephalopathy etc.,
4. Our study showed that Alcoholism is the most common cause for cirrhosis followed by viral hepatitis.

5. Whether the medical treatment improves the HRS not yet studied. This has to be assessed by future studies.

## BIBLIOGRAPHY

1. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31–41.

2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis. 2002;39:S1–266.

3. Froissart M, Rossert J, Jacquot C, Paillard M, Houillier P. Predictive performance of the modification of diet in renal disease and Cockcroft-Gault equations for estimating renal function. J Am Soc Nephrol. 2005;16:763–73.

4. Kyhse-Andersen J, Schmidt C, Nordin G, Andersson B, Nilsson-Ehle P, Lindström V, et al. Serum cystatin C, determined by a rapid, automated particle-enhanced turbidimetric method, is a better marker than serum creatinine for glomerular filtration rate. Clin Chem. 1994;40:1921–6.

5. Jung K, Jung M. Cystatin C: A promising marker of glomerular filtration rate to replace creatinine. Nephron. 1995;70:370–1.

6. Kim KE, Onesti G, Ramirez O, Brest AN. Creatinine clearance in renal disease. A reappraisal. Br Med J. 1969;4:11.

7. Randers E, Erlandsen EJ, Pedersen OL, Hasling C, Danielsen H. Serum cystatin C as an endogenous parameter of the renal function in patients with normal to moderately impaired kidney function. Clin Nephrol. 2000;54:203–9.

8. Randers E, Kristensen JH, Erlandsen EJ, Danielsen H. Serum cystatin C as a marker of the renal function. Scand J Clin Lab Invest. 1998;58:585–92.

9. Newman DJ, Thakkar H, Edwards RG, Wilkie M, White T, Grubb AO, et al. Serum cystatin C measured by automated immunoassay: A more sensitive marker of changes in GFR than serum creatinine. Kidney Int. 1995;47:312–8.

10. Knight EL, Verhave JC, Spiegelman D, Hillege HL, de Zeeuw D, Curhan GC, et al. Factors influencing serum cystatin C levels other than renal function and the impact on renal function measurement. Kidney Int. 2004;65:1416–21.

11. Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: A meta-analysis. Am J Kidney Dis. 2002;40:221–6.

12. Ahlström A, Tallgren M, Peltonen S, Pettilä V. Evolution and predictive power of serum cystatin C in acute renal failure. Clin Nephrol. 2004;62:344–50.

13. Hoek FJ, Kemperman FA, Krediet RT. A comparison between cystatin C, plasma creatinine and the Cockcroft and Gault formula for the estimation of glomerular filtration rate. Nephrol Dial Transplant. 2003;18:2024–31.

14. Peralta CA, Shlipak MG, Judd S, Cushman M, McClellan W, Zakai NA, et al. Detection of chronic kidney disease with creatinine, cystatin C, and urine albumin-to-creatinine ratio and association with progression to end-stage renal disease and mortality. JAMA. 2011;305:1545–52.

15. Coll E, Botey A, Alvarez L, Poch E, Quintó L, Saurina A, et al. Serum cystatin C as a new marker for noninvasive estimation of glomerular filtration rate and as a marker for early renal impairment. Am J Kidney Dis. 2000;36:29–34.

16. Garcia-Tsao G, Parikh CR, Viola A. Acute kidney injury in cirrhosis. Hepatology 2008;48:2064–2077

17. Arroyo V, Colmenero J. Ascites and hepatorenal syndrome in cirrhosis: pathophysiological basis of therapy and current management. J Hepatol 2003;38:S69–S89

18. Martin-Llahi M, Pepin MN, Guevara M, et al. Terlipressin and albumin vs. albumin in patients with cirrhosis and hepatorenal syndrome a randomized study. Gastroenterology 2008;134:1352–1359.

19. Cholongitas E, Marelli L, Kerry A, et al. Female liver transplant recipients with the same GFR as male recipients have lower MELD scores—a systematic bias. Am J Transplant 2007;7:685–692

20. Arroyo V, Fernandez J, Gines P. Pathogenesis and treatment of hepatorenal syndrome. Semin Liver Dis 2008;28:81–95

21. Francoz C, Glotz D, Moreau R, Durand F. The evaluation of renal function and disease in patients with cirrhosis. J Hepatol 2010;52(4):605–613

22. Newman DJ, Thakkar H, Edwards RG, et al. Serum cystatin C measured by automated immunoassay: a more sensitive marker of changes in GFR than serum creatinine for glomerular filtration rate. Kidney Int 1995;47:312–318

23. Randers E, Ivarsen P, Erlandsen EJ, et al. Plasma cystatin C as a marker of renal function in patients with liver cirrhosis. Scand J Clin Lab Invest 2002;62:129–134

24.Sjostrom P, Tidman M, Jones I. Determination of the production rate and non-renal clearance of cystatin C and estimation of the glomerular filtration

rate from the serum concentration of cystatin C in humans. Scand J Clin Lab Invest 2005;65:111–124

25. Demirtas S, Bozbas A, Akbay A, Yavuz Y, Karaca L. Diagnostic value of serum cystatin C for evaluation of hepatorenal syndrome. Clin Chim Acta 2001;2:81–89

26. Gerbes AL, Gulberg V, Bilzer M, Vogeser M. Evaluation of serum cystatin C concentration as a marker of renal function in patients with cirrhosis of the liver. Gut 2002;50:106–110

27. Wiesner R, Edwards E, Freeman R. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology 2003;124:91–96

28. Gault MH, Longerich LL, Harnett JD, Wesolowski C. Predicting glomerular function from adjusted serum creatinine. Nephron 1992;62(3):249–256

29. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 1999;130(6):461–470

30. Salerno F, Camma C, Enea M, Rossle M, Wong F. Transjugular intrahepatic portosystemic shunt for refractory ascites: a meta-analysis of individual patient data. Gastroenterology 2007;133:825–834

31. Yang X, Wang H, Wang Z, Dong M. Alteration and significance of serum cardiac troponin I and cystatin C in preeclampsia. Clin Chim Acta 2006;374:168–169

32. Papadakis MA, Arieff AI. Unpredictability of clinical evaluation of renal function in cirrhosis. Prospective study. Am J Med 1987;82:945–952

33. Woitas RP, Stoffel-Wagner B, Flommers S, et al. Correlation of serum concentrations of cystatin C and creatinine to inulin clearance in liver cirrhosis. Clin Chem 2000;46:712–715

34. Demirtas S, Bozbas A, Akbay A, Yavuz Y, Karaca L. Diagnostic value of serum cystatin C for evaluation of hepatorenal syndrome. Clin Chim Acta 2001;311(2):81–89

35. Berenguer-Pina JJ, Noguera J, Canizares F, et al. Cystatin C: a marker of glomerular filtration rate in liver transplantation. Transplant Proc 2002;34:268–269

36. Orlando R, Mussap M, et al. Diagnostic value of plasma Cystatin C as a glomerular filtration marker in decompensated liver cirrhosis. Clin Chem 2002;48:850–858

37. Sharma P, Schaubel DE, Sima CS, Merion RM, Lok AS. Re-weighting the model for end-stage liver disease score components. Gastroenterology 2008;135:1575–1581

38. Durand F, Valla D. Assessment of prognosis of cirrhosis. Semin Liver Dis 2008;28:110–122

39. Kim JH, Lee JS, Lee SH, et al. The association between the serum sodium level and the severity of complications in liver cirrhosis. Korean J Intern Med 2009;24(2):106–112

40. Angeli P, Wong F, Watson H, Gines P. Hyponatremia in cirrhosis: results of a patient population survey. Hepatology 2006;44:1535–1542

41. Wong VW, Chim AM, Wong GL, Sung JJ, Chan HL. Performance of the new MELD-Na score in predicting 3-month and 1-year mortality in Chinese patients with chronic hepatitis B. Liver Transpl 2007;13:1228–1235

42. Fernandez-Esparrach G, Sanchez-Fueyo A, Gines P, et al. A prognostic model for predicting survival in cirrhosis with ascites. J Hepatol 2001;34:46–52

43. Londono MC, Cardenas A, Guevara M, et al. MELD score and serum sodium in the prediction of survival of patients with cirrhosis awaiting liver transplantation. Gut 2007;56:1283–1290

44. Terg R, Gadano A, Cartier M, et al. Serum creatinine and bilirubin predict renal failure and mortality in patients with spontaneous bacterial peritonitis: a retrospective study. Liver Int 2009;29:415–419

45. Huo TI, Lee SD, Lin HC. Selecting an optimal prognostic system for liver cirrhosis: the model for end-stage liver disease and beyond. Liver Int 2008;28:606–613

46. Knight EL, Verhave JC, Spiegelman D, et al. Factors influencing serum cystatin C levels other than renal function and the impact on renal function measurement. Kidney Int 2004;65:1416–1421

47. Risch L, Huber AR. Glucocorticoids and increased serum cystatin C concentrations. Clin Chim Acta 2002;320:133–134

48. Arabi Y, Ahmed QAA, Haddad S, Aljumah A, Al-Shimemeri A. Outcome predictors of cirrhosis patients admitted to the intensive care unit. *European Journal of Gastroenterology and Hepatology*. 2004;16(3):333–339.

49. Cholongitas E, Calvaruso V, Senzolo M, et al. RIFLE classification as predictive factor of mortality in patients with cirrhosis admitted to intensive care unit. *Journal of Gastroenterology and Hepatology*. 2009;24(10):1639–1647.

50. Francoz C, Glotz D, Moreau R, Durand F. The evaluation of renal function and disease in patients with cirrhosis. *Journal of Hepatology*. 2010;52(4):605–613.

51. Ustundag Y, Samsar U, Acikgoz S, et al. Analysis of glomerular filtration rate, serum cystatin C levels, and renal resistive index values in cirrhosis patients. *Clinical Chemistry and Laboratory Medicine*. 2007;45(7):890–894.

52. Cholongitas E, Marelli L, Kerry A, et al. Different methods of creatinine measurement significantly affect MELD scores. *Liver Transplantation*. 2007;13(4):523–529

53. Belcher JM, Garcia-Tsao G, Sanyal A, et al. Association of AKI with mortality and complications in hospitalized patients with cirrhosis. *Hepatology*. 2012;57(2):753–762.

54. Soto K, Coelho S, Rodrigues B, et al. Cystatin C as a marker of acute kidney injury in the emergency department. *Clinical Journal of the American Society of Nephrology*. 2010;5(10):1745–1754

55. Herget-Rosenthal S, Marggraf G, Hüsing J, et al. Early detection of acute renal failure by serum cystatin C. *Kidney International*. 2004;66(3):1115–1122.

56. Nejat M, Pickering JW, Walker RJ, Endre ZH. Rapid detection of acute kidney injury by plasma cystatin C in the intensive care unit. *Nephrology Dialysis Transplantation*. 2010;25(10):3283–3289.

57. Zappitelli M, Krawczeski CD, Devarajan P, et al. Early postoperative serum cystatin C predicts severe acute kidney injury following pediatric cardiac surgery. *Kidney International*. 2011;80(6):655–662.

58. Haase M, Bellomo R, Devarajan P, et al. Novel biomarkers early predict the severity of acute kidney injury after cardiac surgery in adults. *Annals of Thoracic Surgery*. 2009;88(1):124–130.

**CASE REPORT FORM/PROFORMA**

NAME

AGE

SEX

COMPLETE DIAGNOSIS

TYPE OF HRS

RISK FACTORS FOR DCLD

DIAGNOSTIC INVESTIGATION

CBC,

RFT, RBS, electrolytes

LFT, PT, INR

**Cystatin C**

Urine Analysis

Viral Markers (HBsAg, Anti HCV)

Sr. Uric acid

USG Abdomen

ECG, X-ray chest

OGD scopy

## Informed consent- ‘A study on parameters of Hepatorenal Dysfunction in Cases of DCLD at a Tertiary Care Centre’

Place of study: Govt. Stanley medical college, Chennai

I ……. have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I agree to collect samples of blood/saliva/urine/tissue if study needs.

I understand that I can withdraw from the study at any point of time and even then, I can receive the medical treatment as usual.

I understand that I will not get any money for taking part in the study.

I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full cooperation for this study.

| | |
|---|---|
| Volunteer: | Witness: |
| Name and address | Name and address |
| Signature/thumb impression: | Signature/thumb impression |
| Date: | Date: |

## Informed consent- ‘A study on parameters of Hepatorenal Dysfunction in Cases of DCLD at a Tertiary Care Centre’

நான் இந்த ஆராய்ச்சியில் விவரங்களை மற்றும் புரிந்தது கொண்டேன். ஆய்வில் பங்கு எடுத்தபோது, சாத்தியமான அபாயங்கள் மற்றும் பயன்களை பற்றி நான் அறிந்துள்ளேன்.

நான் எந்தவொரு வேளையிலும் ஆய்வில் இருந்து திரும்ப முடியும், அதன் பின்னர், நான் வழக்கம் போல மருத்துவ சிகிச்சை பெற முடியும் என்று புரிந்து கொள்கிறேன்.

நான் ஆய்வில் பங்கு எடுத்து பணம் எதையும் பெற முடியாது என்று அறிந்துள்ளேன். இந்த ஆய்வின் முடிவுகள் எந்த மெடிக்கல் ஜர்னலில் வெளியிடப்பட இருந்தால் நான் எதிர்க்கவில்லை, என் தனிப்பட்ட அடையாளத்தை வெளிப்படுத்தப்பட்டு இருக்காது.

நான் இந்த ஆய்வில் பங்கெடுப்பதன் மூலம் நான் என்ன செயயபோகிறேன் என்று தெரியும். நான் இந்த ஆய்வில் என் முழு ஒத்துழைப்பையும் கொடுப்பேன் என்று உறுதியளிக்கிறேன்.

**தன்னார்வலர்** **சாட்சி**

பெயர்மற்றும்முகவரி பெயர்மற்றும்முகவரி

கையொப்பம் /விரல்ரேகை: கையொப்பம் / விரல்ரேகை:

ஆராய்ச்சியாளராககையொப்பம்மற்றும்தேதி

| Sr.No. | Age | Sex | Alcoholism | Hepatitis B | Hepatitis C | Metabolic Liver disease | Autoimmune Hepatitis | HRS Type I | HRS Type II | Cystatin C | Serum Creatinine | GRF | Child Pauck score >10 | UGI Bleed | Hepatitic encephalopathy | Coagulopathy | SBP |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 56 | M | YES | NO | NO | NO | NO | YES | NO | 1.8 | 1.5 | 78.2 | NO | NO | YES | YES | YES |
| 2 | 45 | M | YES | NO | NO | NO | NO | YES | NO | 2.3 | 1.6 | 75.2 | NO | NO | NO | NO | NO |
| 3 | 44 | M | YES | NO | NO | NO | NO | YES | NO | 2.6 | 1.7 | 82.1 | NO | NO | NO | NO | NO |
| 4 | 36 | M | YES | NO | NO | NO | NO | NO | YES | 5.8 | 2.5 | 53.5 | YES | YES | YES | NO | NO |
| 5 | 37 | M | YES | NO | NO | NO | NO | YES | NO | 4.6 | 2.9 | 83.1 | NO | NO | NO | NO | NO |
| 6 | 34 | M | YES | NO | NO | NO | NO | YES | NO | 2.9 | 1.8 | 86.1 | NO | NO | YES | NO | YES |
| 7 | 38 | M | NO | YES | NO | NO | NO | YES | NO | 1.6 | 1.9 | 84.1 | YES | NO | NO | NO | NO |
| 8 | 39 | M | NO | NO | YES | NO | NO | YES | NO | 3.2 | 1.5 | 78.1 | NO | YES | NO | NO | NO |
| 9 | 34 | M | YES | NO | NO | NO | NO | YES | NO | 3.1 | 1.4 | 75.1 | NO | NO | YES | YES | NO |
| 10 | 42 | M | YES | NO | NO | NO | NO | YES | NO | 2.9 | 1.8 | 74.1 | NO | NO | NO | NO | NO |
| 11 | 48 | M | YES | NO | NO | NO | NO | NO | YES | 4.7 | 2.6 | 54.3 | YES | NO | NO | NO | NO |
| 12 | 42 | M | YES | NO | NO | NO | NO | NO | YES | 4.8 | 2.7 | 58.3 | YES | YES | NO | NO | NO |
| 13 | 43 | M | NO | YES | YES | NO | NO | NO | YES | 5.2 | 2.8 | 51.1 | YES | YES | YES | YES | NO |
| 14 | 45 | M | NO | NO | NO | NO | NO | YES | NO | 3.2 | 2 | 78.1 | NO | NO | NO | NO | NO |
| 15 | 38 | M | YES | NO | NO | NO | NO | YES | NO | 3.1 | 2.1 | 79.1 | NO | NO | NO | NO | NO |
| 16 | 49 | M | YES | NO | NO | WILSONS | NO | YES | NO | 2.9 | 1.8 | 80.2 | NO | NO | NO | NO | NO |
| 17 | 56 | M | YES | NO | NO | NO | NO | NO | YES | 4.8 | 2.5 | 57.9 | YES | YES | YES | NO | NO |
| 18 | 54 | M | YES | NO | NO | NO | NO | NO | YES | 4.1 | 2.4 | 56.3 | YES | YES | NO | NO | NO |
| 19 | 60 | M | YES | NO | NO | WILSONS | NO | NO | YES | 5 | 2.3 | 57.9 | YES | NO | NO | NO | YES |
| 20 | 38 | M | YES | NO | NO | NO | NO | YES | NO | 1.6 | 1.9 | 82.1 | NO | NO | NO | NO | NO |
| 21 | 36 | M | YES | NO | NO | NO | NO | YES | NO | 1.7 | 1.7 | 81.1 | NO | NO | NO | NO | NO |
| 22 | 34 | M | YES | NO | NO | NO | NO | YES | NO | 1.8 | 1.8 | 78.8 | NO | NO | YES | YES | NO |
| 23 | 44 | M | YES | NO | NO | NO | NO | YES | NO | 2.1 | 1.5 | 77.7 | NO | NO | NO | NO | NO |
| 24 | 46 | M | YES | NO | NO | NO | NO | YES | NO | 1.2 | 2.1 | 76.1 | NO | NO | NO | NO | NO |
| 25 | 47 | M | NO | YES | NO | NO | NO | YES | NO | 2.8 | 2.2 | 74.8 | NO | YES | YES | NO | NO |
| 26 | 32 | M | NO | YES | NO | NO | NO | YES | NO | 2.8 | 2.1 | 79.7 | NO | NO | NO | NO | NO |

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 27 | 29 | M | YES | NO | NO | NO | NO | YES | NO | 3.2 | 2.3 | 72.1 | YES | NO | NO | NO | YES |
| 28 | 30 | M | YES | NO | NO | NO | NO | YES | NO | 3.3 | 1.9 | 74.1 | NO | NO | NO | YES | NO |
| 29 | 28 | M | YES | NO | NO | NO | NO | YES | NO | 3.5 | 2.8 | 69.1 | NO | NO | NO | NO | NO |
| 30 | 40 | M | YES | NO | NO | NO | NO | YES | NO | 3.6 | 1.8 | 70.1 | NO | NO | NO | NO | NO |
| 31 | 42 | M | YES | NO | YES | NO | NO | YES | NO | 2.9 | 1.6 | 71.2 | NO | NO | NO | NO | NO |
| 32 | 44 | M | YES | NO | NO | WILSONS | NO | YES | NO | 1.2 | 2.1 | 64.2 | NO | YES | YES | NO | NO |
| 33 | 36 | M | YES | NO | NO | NO | NO | YES | NO | 3.1 | 2.2 | 69.1 | NO | NO | NO | NO | NO |
| 34 | 38 | M | NO | YES | NO | NO | NO | YES | NO | 3.4 | 2.3 | 74.2 | NO | NO | NO | NO | YES |
| 35 | 42 | M | YES | NO | NO | NO | NO | YES | NO | 0.8 | 2.1 | 78.1 | NO | NO | NO | NO | NO |
| 36 | 41 | M | YES | NO | NO | NO | NO | YES | NO | 3.6 | 1.9 | 74.2 | NO | NO | NO | NO | NO |
| 37 | 47 | M | YES | NO | NO | NO | NO | NO | YES | 4.7 | 3.4 | 62.1 | YES | YES | YES | YES | NO |
| 38 | 48 | M | YES | NO | NO | NO | NO | NO | YES | 4.8 | 2.6 | 60.1 | YES | YES | YES | YES | YES |
| 39 | 32 | M | YES | NO | NO | NO | NO | NO | YES | 5.2 | 2.7 | 57.8 | YES | NO | NO | NO | NO |
| 40 | 42 | M | YES | NO | NO | NO | NO | YES | NO | 3.8 | 1.8 | 72.1 | NO | NO | NO | NO | NO |
| 41 | 39 | M | YES | YES | NO | NO | NO | YES | NO | 3 | 1.7 | 78.2 | NO | NO | NO | NO | NO |
| 42 | 36 | F | YES | NO | NO | NO | NO | YES | NO | 3.1 | 1.6 | 72.1 | NO | NO | YES | YES | NO |
| 43 | 38 | F | NO | YES | NO | NO | NO | YES | NO | 1.2 | 2.1 | 73.8 | NO | NO | NO | NO | NO |
| 44 | 50 | F | NO | YES | NO | NO | NO | YES | NO | 2.8 | 1.5 | 74.2 | NO | YES | NO | NO | NO |
| 45 | 56 | F | NO | NO | YES | NO | NO | YES | NO | 2.7 | 1.5 | 74.8 | NO | NO | NO | YES | NO |
| 46 | 34 | F | NO | NO | NO | NO | YES | YES | NO | 2.8 | 1.6 | 75.3 | NO | NO | NO | NO | NO |
| 47 | 40 | F | YES | YES | NO | NO | NO | YES | NO | 3.1 | 1.6 | 68.2 | NO | NO | NO | NO | NO |
| 48 | 42 | F | NO | NO | NO | NO | NO | NO | YES | 4.8 | 3.2 | 57.2 | YES | NO | NO | NO | NO |
| 49 | 38 | F | NO | NO | NO | WILSONS | NO | NO | YES | 4.1 | 3.1 | 54.5 | YES | YES | YES | NO | YES |
| 50 | 41 | F | NO | NO | NO | NO | YES | NO | YES | 5 | 2.9 | 53.2 | YES | YES | NO | NO | NO |

URKUND

# Urkund Analysis Result

**Analysed Document:** VIJAYARAJAN thesis ROL-1.docx (D31634069)
**Submitted:** 10/24/2017 4:18:00 PM
**Submitted By:** krajanvijay94@gmail.com
**Significance:** 2 %

## Sources included in the report:

Dr.Anandh.doc (D31122078)
Dr.Anandh-1.doc (D31176098)
Influence of beta blockers on complications of cirrhosis_Final.docx (D29028880)
A STUDY OF HYPONATREMIA IN CIRRHOSIS LIVER.docx (D31101988)
THESIS.docx (D31037108)
http://www.aafp.org/afp/2006/0901/p767.html

## Instances where selected sources appear:

6

## CERTIFICATE

This is to certify that this dissertation work titled **"A study on parameters of Hepatorenal Dysfunction in cases of DCLD at a Tertiary Care Centre''** of the candidate **Dr.K.VIJAYARAJAN** with registration Number **201511065** for the award of **M.D. in the branch of GENERAL MEDICINE** . I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **2 percentage of plagiarism** in the dissertation.

Guide & Supervisor sign with Seal.

## ABBREVIATIONS

DCLD – Decompensated Liver Disease

HRS-Hepato Renal Syndrome

AKI-Acute Kidney Injury

UGI-Upper Gastro Intestinal

HE- Hepatic Encephalopathy

MDRD-Modified Diet Renal Disease

eGFR-estimated glomerular filtration rate

CysC-CystatinC

GIT-gastrointestinal tract

OGD-Oesophago Gastro Duodenoscopy